

*Sixth Special Report  
to the U.S. Congress on*

# ALCOHOL AND HEALTH

*From the Secretary of  
Health and Human Services*

*January 1987*

**U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES**  
Public Health Service  
Alcohol, Drug Abuse, and Mental Health Administration  
National Institute on Alcohol Abuse and Alcoholism

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National Institute on Alcohol Abuse  
and Alcoholism  
5600 Fishers Lane  
Rockville, Maryland 20857**

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(NIAAA)

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# Foreword

For 15 years, the Special Reports on Alcohol and Health have provided the U.S. Department of Health and Human Services and its forerunner, the Department of Health, Education, and Welfare, with the opportunity to report to the Congress and to the American people on our progress toward understanding alcohol abuse and alcoholism, problems that significantly threaten the common good. The *Sixth Special Report to the U.S. Congress on Alcohol and Health* continues this important task. It contains ample evidence that our understanding of alcohol-related problems continues to increase and that this growing body of knowledge has the potential to alter significantly the ways that we prevent and treat alcohol abuse and alcoholism. It is particularly opportune that the issuance of this report occurs at a time when Americans appear increasingly aware of the impact of alcohol abuse and alcoholism on their health and economic and social well-being and are beginning to seek ways to contain it.

Prompted, perhaps, by the growing number of well-known individuals who have chosen to speak out about their alcohol and other drug problems and the role of treatment in their recovery, the stigma of alcoholism is slowly diminishing. Heightened attention in the media on the dangers and tragedies of drinking and driving or perhaps the growing awareness of the relationship between lifestyle and health has aided in increasing public awareness of the health-related, economic, and social consequences of alcoholic beverage consumption.

Whatever the reasons, it appears that citizens and their communities are beginning to seek out information to help them better understand the impact of alcohol-related problems and to assist in initiating alcohol prevention and education activities. We are also beginning to see hopeful signs that individuals are altering their lifestyles to reduce their risk for alcohol-related problems. For example, per capita consumption of alcohol has shown a significant decline since its peak in 1980–81, dropping from 2.76 gallons of pure alcohol per person 14 years old and older in 1978 to 2.65 gallons in 1984. Alcohol-related traffic accidents have also decreased. Although there may be a number of explanations for these decreases, among them may be increasing public concern about health in general and growing public intolerance for drinking and driving as acceptable behavior.

Of great importance to me personally is the unique role that alcohol plays with our youth. We know that early alcohol use increases the risk for our children's later development of alcohol-related problems, we know that alcohol use by our youth greatly increases the chances that these youngsters will use other drugs, and we know that alcohol increases the risk for a range of problem behaviors—for example, suicide and homicide—which affect the very lives of our next generations. We also know that many of these problems can be prevented if we teach our children how to say no to alcohol and other drugs. For many, many years, we have accepted—or at a minimum tolerated—alcohol use by older adolescents as an expected “rite of passage” to adulthood. I am hopeful that the

movement to teach our children refusal skills continues to gain momentum and that those within our society who interact with youth—educators, the religious community, those involved with youth sports activities, the medical community, and particularly parents—communicate to these vulnerable young people that alcohol use by under-age youth is not an appropriate activity.

Although the problems of alcohol abuse and alcoholism remain enormous, there is hope in the fact that as a country we are beginning to find that we need not be defenseless against them. Each of us working in our communities and with our employers, families, and friends can bring about fundamental changes in attitudes and behaviors associated with alcohol use and in doing so can provide for the health and well-being of our future generations.

*Otis R. Bowen, M.D.*

*Secretary, Health and Human Services*

# Preface

Active Federal involvement in the alcoholism field has had a relatively short history. Landmark legislation passed by the Congress in 1970 initiated Federal involvement and leadership in combating the problems of alcohol abuse and alcoholism by authorizing the creation of the National Institute on Alcohol Abuse and Alcoholism (NIAAA). The new Institute, charged with fostering research and disseminating information on alcohol abuse and alcoholism, began operations the following year. The legislation that created the NIAAA requires it to provide Congress and the public with periodic special reports on the state of knowledge about alcohol and its effects on health. The first such report was published in 1971, during the NIAAA's first year of operation. This year marks the NIAAA's 15th anniversary, and this is the *Sixth Special Report to the U.S. Congress on Alcohol and Health*.

The Special Reports on Alcohol and Health, as a whole, serve as historical reference points and current documentaries of our progress in understanding the effects of alcohol on health and our ability to use this knowledge to prevent and treat alcohol-related problems.

For example, 15 years ago the *First Special Report to the U.S. Congress on Alcohol and Health* provided a discussion of then current theories on the causes of alcoholism. According to the discussion concerning genetics, "the evidence thus far for a genetic inheritance of alcoholism is unsatisfactory. The possibility that humans may inherit a predisposition for alcoholism or an immunity to it, however, has not been ruled out." The *Second Special Report* in 1974 and the *Third Special Report* in 1978 reported on new studies of twins for inheritance of alcoholism, acknowledged that a genetic predisposition was probable, but concluded that "evidence establishing this was not regarded as conclusive." No new advances in the study of the heritability of alcoholism were reported in the 1981 *Fourth Special Report*. However, the *Fifth Special Report*, issued in 1983, stated unequivocally that "a substantial body of animal and human research now leaves little question that heredity plays a role in susceptibility to some of alcohol's effects and in some individuals increases their likelihood to becoming dependent on it."

Today, of course, through increasing knowledge of the biological antecedents of alcoholism, we know that alcoholism, like other diseases, has many forms and results from a complex interplay of genetic and environmental factors involved in its development. Exciting advances in our knowledge concerning genetic components to alcoholism and ways in which this knowledge can lead to the development of prevention and treatment strategies are discussed in the *Sixth Special Report*, which is concerned primarily with new information that has come to light since the *Fifth Special Report*.

In addition to their primary function of providing an up-to-date knowledge base on alcohol and health, the Special Reports on Alcohol and Health fulfill a variety of other functions. Alcohol has diverse effects—biological, psychological, and social—and this diversity is reflected in



the range of professions that are required to deal with alcohol abuse and alcoholism. These reports allow scientists, clinical personnel, program managers, and others involved in alcohol-related activities to have a common base of knowledge upon which to develop policies and programs to prevent and treat alcohol abuse and alcoholism. They also provide specialists who are indirectly concerned with one or another aspect of alcohol-related problems—from medical schools, primary health care facilities, social services agencies, private insurance businesses, and a variety of other areas—with information to keep abreast of general progress in the alcohol field. Finally, because these reports are widely read by general audiences, they serve the ultimate purposes of increasing public understanding of alcohol-related problems and stimulating action by citizen groups and others to prevent and reduce them.

The *Sixth Special Report to the U.S. Congress on Alcohol and Health* provides a vital link between what was, what is, and what could be. It deserves to be read not only by everyone who is concerned about alcohol abuse and alcoholism but also by all who are concerned for the future health of all Americans.

*Robert E. Windom, M.D.*  
*Assistant Secretary for Health*



# Acknowledgments

**T**he *Sixth Special Report to the U.S. Congress on Alcohol and Health* is the product of the collaboration of many people. Scientists and science writers, guided by an Editorial Board, worked closely together to produce this report. The scientists assisted the writers by recommending research articles, reviewing each draft, and suggesting changes. The writers reviewed and summarized thousands of articles.

Some of the world's most distinguished scientists, alcoholism researchers, and medical authorities were involved in preparing this report; many of them also contributed to previous reports. The scientists' and writers' uncompromising commitment to scientific accuracy is reflected in every chapter of this report.

## CONTRIBUTORS

Henri Begleiter, Ph.D.  
SUNY—Health Science Center  
Brooklyn, New York

Floyd E. Bloom, M.D.  
Scripps Clinic and Research  
Foundation BCR-1  
La Jolla, California

Nelson Butters, Ph.D.  
San Diego Veterans Administration  
Medical Center  
University of California  
San Diego, California

Raul Caetano, M.D., Ph.D.  
Alcohol Research Group  
Medical Research Institute of  
San Francisco  
University of California  
School of Public Health  
Berkeley, California

Sterling K. Clarren, M.D.  
Department of Pediatrics  
University of Washington  
Seattle, Washington

C. Robert Cloninger, M.D.  
Washington University Medical  
Center  
St. Louis, Missouri

Norman Giesbrecht, Ph.D.  
Addiction Research Foundation  
Toronto, Ontario  
Canada

Ralph Hingson, Sc.D., M.P.H.  
Section of Socio-Medical  
Sciences & Community Medicine  
Boston University School  
of Public Health  
Boston, Massachusetts

Harold Holder, Ph.D.  
Prevention Research Center  
Berkeley, California

Richard Jessor, Ph.D.  
Institute of Behavioral Science  
University of Colorado  
Boulder, Colorado

Louis G. Lange, M.D., Ph.D.  
Division of Cardiology  
Jewish Hospital  
Washington University School of  
Medicine  
St. Louis, Missouri

Ting-Kai Li, M.D.  
School of Medicine & Veterans  
Administration Medical Center  
Indiana University  
Indianapolis, Indiana

Jack Mendelson, M.D.  
McLean Hospital  
Belmont, Massachusetts

Esteban Mezey, M.D.  
The Johns Hopkins Hospital  
Baltimore, Maryland

Sheldon Miller, M.D.  
University of Medicine &  
Dentistry of New Jersey  
New Jersey Medical School  
Newark, New Jersey

James Mosher, J.D.  
Prevention Research Center  
Berkeley, California

Carrie L. Randall, Ph.D.  
Veterans Administration Hospital  
Medical University of South Carolina  
Charleston, South Carolina

Judy Roizen  
Institute for Social and  
Administrative Studies  
The University of the South Pacific  
Suva, Fiji

Paul M. Roman, Ph.D.  
Institute of Behavioral Research  
University of Georgia  
Athens, Georgia

Robin Room, Ph.D.  
Alcohol Research Group  
Berkeley, California

Emanuel Rubin, M.D.  
Jefferson Medical College of  
Thomas Jefferson University  
Philadelphia, Pennsylvania

Marcia Russell, Ph.D.  
Research Institute of Alcoholism  
Buffalo, New York

Robert J. Sokol, M.D.  
Department of Obstetrics and  
Gynecology  
Hutzel Hospital  
Wayne State University  
Detroit, Michigan

Robert Straus, Ph.D.  
Department of Behavioral Science  
College of Medicine  
University of Kentucky  
Lexington, Kentucky

Alexander C. Wagenaar, Ph.D.  
Transportation Research Institute  
Department of Injury Analysis  
and Prevention  
University of Michigan  
Ann Arbor, Michigan

Don Walker, Ph.D.  
Department of Neuroscience  
College of Medicine and Veterans  
Administration Medical Center  
University of Florida  
Gainesville, Florida

John Wallace, Ph.D.  
Edgehill Newport  
Newport, Rhode Island

Lawrence Wallack, Dr. P.H.  
School of Public Health  
University of California  
Berkeley, California

Diana Chapman Walsh, Ph.D.  
Health Policy Institute and  
School of Public Health  
Boston University  
Boston, Massachusetts

## EDITORIAL BOARD

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Rockville, Maryland

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Office of Scientific Affairs  
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Abuse and Alcoholism  
Rockville, Maryland

## WRITERS, EDITORS, AND REVIEWERS

The lead writer and editor of the *Sixth Special Report* was Peter L. Petrakis, Ph.D. Writers of the individual chapters were Bevin Jane Grylack, Ph.D.; Alice Harvey; Barbara Hyde; Anne Nauman; Bettina M. Scott, Ph.D.; Julia Stam; and John Wallace, Ph.D. This report was prepared under the direction of Joan Hurley and Janet Horwitz.

A significant number of NIAAA staff made major contributions to this report through technical review and consultation. In addition to Loran D. Archer, Deputy Director, they include Darryl Bertolucci; Lois Chatham, Ph.D.; Paul Collins; Robert Denniston; Mary Dufour, M.D.; Susan Farrell; William Gregory; Brenda Hewitt; John Noble; Claude Reeder; Walter Schaffer, Ph.D.; Boris Tabakoff, Ph.D.; Leland Towle; Ernestine Vanderveen, Ph.D.; and Kenneth Warren, Ph.D.



# A Note

**T**he *Sixth Special Report on Alcohol and Health* is the result of the labors of many people. Contributions from a large number of distinguished scientists throughout the Nation provided important basic resource documents. Other distinguished scientists served as writers and reviewers of the individual chapters and as members of the Editorial Review Board. These persons are acknowledged elsewhere in this document and to this acknowledgment I add my personal thanks for their assistance.

A number of other individuals, also acknowledged elsewhere in this document, spent many long hours writing and editing the Report to ensure the completeness and accuracy of its information and tending to the many necessary, but often overlooked, details involved in conforming to the high standards of reports issued by the Department of Health and Human Services. To these persons I also extend my appreciation for their assistance in producing a document that well reflects the time and effort spent in quality control.

Lastly, but most importantly, my special acknowledgment and thanks go to Loran D. Archer, Deputy Director of the National Institute on Alcohol Abuse and Alcoholism (NIAAA), for his efforts in guiding the development and preparation of this report while serving as Acting Director of NIAAA. A major part of the work on the *Sixth Special Report* was accomplished prior to my appointment as NIAAA Director. Mr. Archer's expert guidance of the process throughout its developmental stages allowed me to focus on the "finishing touches" to an already excellent document, a welcome task for an incoming Director.

I am pleased to have been a part of this process and hope that the *Sixth Special Report to the U.S. Congress on Alcohol and Health* is given the serious attention that it merits.

*Enoch Gordis, M.D.*

*Director*

*National Institute on Alcohol  
Abuse and Alcoholism*

# Introduction

The history of alcohol-related problems is as old as the history of alcohol use, and success in preventing or otherwise ameliorating these problems has been an elusive goal. Until fairly recently, research on alcohol abuse and alcoholism was circumscribed by the view of alcoholism as an area more likely to respond to moral imperatives than to scientific inquiry. Today, alcohol research is joining the mainstream of scientific pursuit and, over the past two decades, our knowledge of the biological and psychosocial effects of alcohol has been steadily expanding. Further, while eliminating alcohol-related problems remains a hope for the future, we are beginning to witness the beginnings of change in the public understanding and awareness of the risks associated with alcohol use.

The Special Reports on Alcohol and Health provide us with a unique opportunity to assess where we have been, where we are, and how much farther we must go to prevent and reduce alcohol-related problems. That we continue to make steady progress is evident in the findings cataloged in these reports over the years. That alcohol abuse and the disease of alcoholism continue to be substantial public health problems can be seen as well.

In research, we have witnessed the progression of alcohol-related studies from the empirical to the theoretical—from the observation of what happens to research designed to understand why it happens. We are gaining new knowledge in areas such as the biological antecedents of alcoholism and how these are affected by various environmental factors; the multiple factors surrounding individual susceptibility to alcohol abuse and dependence; the multiple forms in which alcohol-related problems are manifested; and the neurochemical basis of the alcohol addiction process. We also are beginning to refine our survey methods to provide reliable information on the nature and extent of alcohol-related problems in the many diverse populations that the United States comprises.

Although public concern about alcohol-related problems has not yet reached the point where pressure to discover causes and to develop preventive measures and effective treatment rivals its concern in other areas such as cancer and heart disease, we see evidence of a growing awareness of the link between alcohol use and health. Over the past few years, we also have seen modest declines in a number of alcohol-related problem indicators, including alcohol-related traffic accidents, consumption of alcoholic beverages, deaths from alcohol-related liver disease, and alcohol use by adolescents.

It is always easiest to tell the “good news.” A more difficult task is to acknowledge that what has been achieved thus far is just a beginning. For example, while alcohol-related traffic accidents have declined, such accidents continue to claim over 18,000 lives each year in the United States. Deaths from cirrhosis of the liver, most often caused by alcohol abuse and alcoholism, are down, but cirrhosis continues to be the ninth leading cause of death in this country. Although there is evidence of modest declines in the use of alcohol by underage youth, alcohol remains the most widely used drug among American youth in 1986.

Large numbers of underage youth drink heavily and consistently, and an estimated 30 percent, or 4.6 million adolescents, experience negative consequences of alcohol use (such as poor school performance, trouble with parents, or involvement with law enforcement personnel). More than one out of every three high school seniors reports drinking heavily—five or more drinks in a row during the prior 2 weeks—and nearly 5 percent of high school seniors report drinking daily.

As in other health areas, our field's ability to bring about significant changes in these and other problem indicators requires time, patience, and continued effort to resolve its fundamental questions. At present, the answer to the central question in the alcohol field—the pathological appetite for alcohol—remains elusive: we still do not know why millions of people cannot stop drinking even though they know they are killing themselves. Research on treatment outcome is vital to learn how to match patients with the most appropriate treatment. One sign of a mature field is its capacity for rigorous self-scrutiny. We are just beginning to emulate other fields such as cancer and heart disease by seeking to validate current treatments for alcoholism. Validating treatment effectiveness will require, among other things, undertaking well-designed clinical trials. However, for these and other studies on treatment outcome to reach their full potential, the development of an objective marker of alcohol consumption is essential.

Better technology for measuring the efficacy of prevention measures must be developed also. It is easy to suggest

plausible prevention measures, such as classroom education at different ages, media campaigns, and community-based education efforts, particularly those which involve parent groups. Evaluating the impact of these measures, however, is difficult, costly, and complex. As a result, we do not understand sufficiently which prevention measures work and with whom they work. Finally, while alcohol use is believed to have severe and debilitating effects on adolescent physical and psychosocial development, insufficient research attention has been paid to this subject.

Looking at the extraordinary breakthroughs in genetics, neuroscience, and other important areas, we might be tempted to believe that all we need now is to expand prevention and treatment services. This would be a mistake. Until we have answered key questions about the pathological appetite for alcohol, and until we can better assess the efficacy of prevention and treatment measures, we will continue to make only limited headway in devising better treatments and in reducing alcohol-related problems. There are no easy answers to these and other questions, but with the immensely talented individuals working in research, prevention, and treatment and with the support of the American people, we can be confident that these crucial challenges will be met.

*Enoch Gordis, M.D.*

*Director*

*National Institute on Alcohol  
Abuse and Alcoholism*



# Alcohol and Health—An Overview

## EPIDEMIOLOGY OF ALCOHOL-RELATED PROBLEMS

In 1984, the estimated consumption of alcoholic beverages in the United States was the equivalent of 2.65 gallons of pure alcohol per person 14 years of age or older. This is the amount of alcohol one would obtain from approximately 50 gallons of beer, 20 gallons of wine, or more than 4 gallons of distilled spirits. This level of consumption is the lowest since 1977, and it reflects the continued gradual decline in per capita consumption that has been underway since 1981. Heavier drinkers, who constitute 10 percent of the drinking population, account for half the alcohol consumed in the United States.

Alcohol is associated with a wide variety of diseases and disorders, but the greatest health hazard from chronic alcohol consumption is liver disease. In 1983, cirrhosis of the liver was the ninth leading cause of death in the United States. Cirrhosis death rates are higher for men than for women and higher for nonwhites than for whites. Cirrhosis mortality has been declining, and the mortality rate for 1983 was the lowest since 1959.

Nearly half of all accidental deaths, suicides, and homicides are alcohol related. Victims are intoxicated in about one-third of drownings, homicides, and boating and aviation deaths and in about one-fourth of suicides. However, there was a significant decrease in the number of alcohol-related traffic fatalities from 1980 to 1984; during that period, the proportion of fatally injured drivers who were legally intoxicated dropped from 50 to 43 percent.

Both alcohol use and drug use (except for cocaine) have declined among high school seniors since 1980. In 1985, 5 percent of high school seniors drank daily. One-third of adolescents aged 16 to 18 report that most or all of their friends drink regularly.

Alcohol use creates problems for an estimated 18 million persons 18 years old and older. These may be alcohol dependence symptoms such as binge drinking or the loss of control over drinking behavior, or they may be negative personal consequences such as problems with health, work, or personal relationships. Nearly half of convicted jail inmates were under the influence of alcohol when they committed the crime, and more than half of them were drunk at the time.

How much an individual drinks, how often he or she does it, and what the response to alcohol exposure will be are determined by complex interactions of demographic, social, economic, and biological factors. Successful prevention and treatment of alcohol abuse and alcoholism must be based on knowledge and understanding of these factors. Age, sex, and ethnic background are significant determinants, as shown below:

- Women drink significantly less than men and have fewer drinking-related problems, but recently there has been an increase in drinking among women aged 35 to 64 years. Higher rates of gynecologic and obstetric problems, including stillbirths and birth defects, are associated with higher drinking levels.



- People over age 65 consume less alcohol than younger adults, possibly because aging reduces tolerance for alcohol, and they have a lower prevalence of alcohol abuse. Elderly long-term alcohol abusers are at high risk for adverse health effects.
- Homeless persons in the United States, estimated to number 250,000 to 350,000, have a high rate of alcohol-related problems. The homeless include growing numbers of women, children, the elderly, the unemployed, minorities, and the mentally ill.
- Drinking patterns vary among ethnic and racial groups in our country. They also vary between the sexes in these groups. Abstinence from alcohol is more common among blacks than among whites, and black men who drink are less likely than white men to drink heavily. However, black women who drink are more likely than white women to drink heavily. The incidence of alcohol-related medical problems, especially liver cirrhosis and cancer of the esophagus, is very high among blacks. Cirrhosis mortality rates for blacks are twice as high as the rates for whites.

Hispanic American men have a higher rate of alcohol use and abuse than the general population. First-generation American-born Hispanics drink more heavily than foreign-born Hispanics. Nearly half of Hispanic women are abstainers, but less than one-fourth of Hispanic men are. There is a high rate of mortality from cirrhosis among Hispanic American men.

American Indians and Alaskan Natives appear to have very high rates of alcohol abuse and alcoholism overall, although many tribes are almost totally abstinent. Alcohol-related illness and injury rates among American Indians are three times higher than in the general population. Among American Indian men, accidents are the second leading cause of death and account for nearly one-fourth of deaths. Homicide and suicide rates are double the rates for the general population. Liver cirrhosis is the fourth leading cause of death among American Indians.

Asian Americans, regardless of national origin, have very low levels of alcohol abuse and alcoholism. Abstinence is very high among Asian Americans, especially Koreans, Chinese, and women of all Asian groups.

## THE GENETICS OF ALCOHOLISM

Evidence for genetic predisposition to alcoholism continues to grow, and it is now widely accepted by researchers in the field that alcoholism can result from the interaction of heredity and environment. Possibly characteristic brain electrical patterns have been found in subjects who are not alcoholic but are judged to be at risk of alcoholism because alcoholism exists among their first-degree relatives.

Studies of individuals who had a biological parent with alcoholism but were removed from the alcoholic environment through adoption at an early age have allowed assessment of the relative contributions of genetic and

environmental factors in the genesis of alcoholism. Such studies have identified two types of genetic predisposition to alcoholism, male-limited and milieu-limited.

- Male-limited susceptibility occurs only in males, is highly heritable, gives rise to severe early-onset alcoholism often requiring extensive treatment, and is associated with serious lawbreaking.
- Milieu-limited susceptibility, which was found to occur in both sexes, is perhaps involved in most cases of alcoholism. This type of hereditary alcoholism has a late onset, is usually not as severe as male-limited alcoholism, and is not associated with the legal system. Milieu-limited susceptibility requires environmental provocation to become expressed as alcoholism, but environmental provocation does not include alcoholism in the adoptive parents. The only significant parental factor found associated with this type of alcoholism in the adoptees was low socioeconomic status of the adoptive father.

This typology, which was based on study of official records, has recently been validated and extended in a clinical population of alcoholics.

Genetic molecular variations in alcohol-metabolizing enzymes are a major area of research on the heredity of alcoholism because a mutation that produces a slight alteration in the molecular structure of these enzymes could be expected to have a pronounced effect on their ability to remove alcohol from the body. Many investigators believe that such studies have the potential of explaining fundamental mechanisms of alcoholism and of identifying genetic markers of susceptibility.

There is considerable evidence that Oriental populations have a very high prevalence of a form of aldehyde dehydrogenase that has a low efficiency in removing acetaldehyde, a toxic compound that is the first product of alcohol metabolism. Rapid accumulation of acetaldehyde, after only a few drinks, produces skin flushing, a rapid pulse, and other uncomfortable symptoms, and this discomfort may deter further drinking. The high prevalence of the gene for this form of the enzyme in Oriental populations may help explain their low rates of alcoholism.

## ALCOHOL AND THE BRAIN

Alcohol can profoundly affect the structure and function of the central nervous system, particularly at the level of the neuronal membrane, where effects are quite selective. One of the principal aims of alcohol-related research on the brain is to correlate neurochemical and anatomic changes with behavioral and physiological responses to alcohol. The use of positron emission tomography and other new noninvasive imaging techniques promises to advance research on functional central nervous system deficits associated with alcohol-induced brain damage.

Alcohol tolerance, physical dependence, and the alcohol withdrawal syndrome appear to be the result of changes within neuronal membranes that are produced by chronic alcohol consumption. Most organic brain damage attributed



to alcohol's effects has been identified in brain areas such as the hippocampus, cerebellum, and locus coeruleus.

Recent studies of memory suggest that the memory system that enables people to retrieve information that is encoded and consolidated is disrupted during alcohol intoxication. Although there is still no proof that moderate alcohol consumption will cause permanent structural brain damage, some evidence suggests that moderate social drinking may compromise cognitive efficiency. The reversibility of alcohol-induced organic brain damage and neuropsychological impairment remains one of the most controversial areas in alcohol-related research.

## OTHER HEALTH EFFECTS

Alcohol has effects of enormous range and complexity throughout the body. Virtually every organ system in the body is affected by alcohol, either directly or indirectly. Research continues to expand our understanding of the consequences of alcohol consumption.

It has long been believed that practically all alcohol is absorbed from the gastrointestinal system and is metabolized mostly in the liver. However, new evidence indicates that alcohol metabolism also occurs in the lining of the stomach. Gastric alcohol metabolism may provide protection against toxicity when moderate amounts of alcohol are consumed. Nevertheless, alcohol consumption can cause gastric lesions, especially when taken with other substances that irritate the stomach, such as aspirin. Alcohol can also affect the small intestine by altering intestinal motility, metabolism, blood circulation, and cellular structure, and it may also cause malabsorption of nutrients.

Although most evidence indicates that development of liver cirrhosis requires the chronic consumption of large amounts of alcohol, newer studies suggest an increased risk in men who drink as little as three drinks a day and in women who drink as little as one and one-half drinks a day.

Myocardial disease related to alcohol consumption occurs in only 1 to 2 percent of chronic abusers of alcohol, but the prognosis for those who develop it is very poor unless they abstain from alcohol. Recent studies also indicate that alcohol has an adverse effect on heart tissue even in young adults.

Several studies indicate that alcohol consumption is associated with hypertension and blood coagulation disorders, but evidence that moderate drinking has a protective effect against coronary heart disease continues to be controversial.

Alcohol has major effects on the endocrine and reproductive systems in both men and women. Alcohol's effects on the adrenocortical hormones may play a role in the development of tolerance and physical dependence. Chronic heavy alcohol consumption in men reduces the levels of circulating testosterone, evidently by direct action on the cells that produce this hormone. One result is the development of female hair patterns and breast enlargement in some male alcoholics. Although the female hormone estradiol is not reduced by alcohol consumption, some alcoholic women develop menstrual disturbances,

infertility, and hormonal imbalances. Some changes in adrenal hormones brought about by chronic alcohol consumption may be permanent. Alcohol has also been shown to have major effects on the levels of thyroid hormones, and there is some evidence that such alterations may be involved in the development of a type of liver necrosis in chronic alcohol abusers.

Chronic alcohol abuse is associated with increased susceptibility to infectious diseases and several kinds of cancer, evidently because of alcohol's ability to interfere with several arms of the immune defense system.

Although our understanding of the medical consequences of alcohol continues to grow, there are many unanswered questions. A major need is for study of the fundamental cellular mechanisms that can explain the enormous range of alcohol's effects throughout the body.

## ALCOHOL AND PREGNANCY

Significant progress is being made in understanding the effects of prenatal alcohol exposure on the developing organism. Specific brain structures that are especially sensitive to alcohol and are involved in functions known to be impaired in the fetal alcohol syndrome are being identified. Animal studies have shown that prenatal alcohol exposure reduces the number of neurons in the hippocampus of the brain and causes certain hippocampal neurons to terminate in abnormal locations. Other studies indicate extreme sensitivity to alcohol of another brain structure, the locus coeruleus. The locus coeruleus is the seat of many behavioral functions known to be abnormal in the fetal alcohol syndrome. There is evidence that the gastrulation stage of embryonic development may be a time of particular vulnerability to alcohol toxicity leading to craniofacial and brain anomalies characteristic of the fetal alcohol syndrome in humans. Gastrulation in humans occurs in the third week of pregnancy, a time when most women are unaware that they are pregnant.

Factors that modify the risk of an alcoholic woman's giving birth to a baby with the fetal alcohol syndrome are being identified. Among the risk-modifying cofactors are number of previous births, race, previous history of alcohol problems in the mother, and beverage type.

A recent study found that sodium acetylsalicylate had a strong protective effect against alcohol-induced fetal malformation and prenatal mortality in mice, possibly as a result of the drug's known ability to interfere with prostaglandin synthesis. This is perhaps the first report of antagonism of alcohol teratogenesis by pharmacological intervention, and it suggests that the prostaglandin system may be a fruitful area of research to understand the underlying mechanisms of alcohol-induced birth defects.

## PREVENTION AND INTERVENTION

Reducing the incidence of alcohol-related problems requires strategies for prevention and strategies for intervention. Prevention strategies focus on those who may not yet drink but are at risk for developing alcohol problems.



Intervention strategies are aimed at encouraging treatment or behavioral change for those who drink heavily, frequently, or under conditions that endanger health, life, or property. Prevention includes education and communication programs to increase public knowledge of alcohol problems, as well as laws and regulations. Intervention focuses on those who already have alcohol problems and involves activities such as training programs on alcoholism for primary health care providers, programs for children at risk, employee assistance programs, and server intervention strategies.

## Prevention

Existing research indicates that mass media campaigns by themselves do not change health behavior, but they can create a context that increases the effectiveness of other strategies to change behavior. They can be effective when combined with other prevention strategies such as increased enforcement of drinking and driving laws.

Although educational programs in schools have increased alcohol and drug knowledge, few have been effective in preventing alcohol abuse or delaying experimentation with alcohol by young children and adolescents. The evaluation literature on many of these programs is methodologically weak, and firm conclusions cannot be drawn from the reported results.

Analysis of alcohol education programs on college campuses is more encouraging. These programs often have strong evaluation designs and use control groups and treatment groups. In general, longer programs (20 to 36 hours) produce longer changes in drinking behavior than shorter programs (2 to 20 hours). However, this positive picture of the effectiveness of college programs has been challenged on the grounds of selection bias, namely, that participants were volunteers highly motivated to change their lifestyles and that the studies did not control for this.

Research on alcoholic beverage advertising suggests that exposure to such advertising is second to peer pressure as a correlate of teenage alcohol consumption, particularly of beer and wine. Also, a nationwide survey of 1,200 respondents indicated that advertising contributes to certain forms of problem drinking.

There is a widespread belief that favorable portrayals of alcohol consumption in the entertainment media can cause increased consumption by viewers. Although the evidence for this is inconclusive, there has been support for limiting drinking scenes in such media and using those media as educational forums for preventing alcohol abuse.

There is evidence that measures to increase the price of alcoholic beverages, such as taxation, reduce consumption. This has been demonstrated in studies in the United States and in other countries. Other studies have found that restricting the availability of alcohol in this manner reduces both per capita consumption and alcohol-related mortality.

Legislation in many States raising the legal drinking age from 18 years to 20 or 21 years has produced marked reductions in alcohol-related traffic accidents, according to several studies. However, evidence that such legislation

has reduced alcohol consumption among young people is less conclusive.

Several studies indicate that traffic accidents and resulting injuries and fatalities are reduced when the probability of detection and punishment for drinking and driving is increased. However, public perception of this probability appears to be a crucial factor. When the public perceives that swift and certain punishment is no longer likely, the drinking and driving incidents increase. Many researchers who are pessimistic about drinking and driving laws as a long-range deterrent believe that a more productive goal is to decrease the injuries and fatalities associated with any form of less than optimal driving, whether caused by alcohol or simply by errors in judgment, i.e., by designing safer automobiles and roads and removing highway hazards.

## Intervention

The problems of alcohol abuse and alcoholism are receiving increased emphasis in medical school curricula, and several professional associations are actively promoting substance abuse education. Although there is evidence that increasing knowledge is changing physicians' attitudes about alcoholics, this may not necessarily lead to changes in clinical practice. There is a great need to assess clinical behavior in evaluating alcohol training for professionals.

Considerable research is being done to develop a simple, accurate screening procedure for early identification of alcohol problems. The two major areas of investigation are biochemical markers and psychosocial indicators. Biochemical markers have been found to be insufficiently discriminating to be of any use in population screening, however, and some investigators think it is unlikely that a single, reliable biochemical marker of alcohol abuse drawn from current standard clinical tests will be found. A mix of biochemical markers and screening interviews and questionnaires to detect psychosocial indicators shows much promise as effective measures for early identification and intervention.

Children of alcoholics are a population at greater risk of developing alcohol problems and are receiving increasing attention from intervention programs. Research is needed to validate some interesting suggestions regarding unique problems faced by this group. The special needs of the children of alcoholics have only recently attracted the attention of experts, and research in this area is not as developed as in some other areas of alcohol research.

The impact of employee assistance programs is difficult for independent investigators to assess because of methodological problems, including the lack of free access to data. However, program practitioners indicate high levels of program success, and the continuing financial support of the programs by employers cannot be ignored as evaluative information. Some investigators, however, question whether these programs do effect changes in drinking habits and job performance among their enrollees.

A new approach to deterring the development of alcohol-related problems, especially alcohol-impaired driving,

is server intervention. The aim of server intervention programs, which have been introduced in several States in recent years, is to reduce alcohol-related problems among drinkers by educating those who serve them drinks. The programs have generally been well received, although they are still too new to have received adequate objective evaluation.

## TREATMENT

The number of people in treatment for alcoholism continues to grow; more than half a million persons were reported to be in treatment in late September 1984. From 1978 to 1984, State and local government control of hospital inpatient treatment declined by 16 percent, and for-profit ownership of such units increased by 392 percent.

The apparent heterogeneity among alcoholics is attracting considerable interest in the field. Efforts are being made to understand and measure this heterogeneity for possible application of the concept to individualized treatment planning.

Pharmacotherapy for alcoholics has not changed dramatically in recent years. There is continuing interest in using disulfiram as an adjunct to more comprehensive treatment for some alcoholics. Lithium carbonate may be a

useful therapy for some alcoholics, mainly those with a coexisting affective disorder.

Both social and medical settings have proved appropriate for safe and effective detoxification of alcoholics. The choice of a social or medical setting for detoxification is determined by factors such as the severity of alcohol dependence and withdrawal symptoms, general medical condition, and psychiatric features.

Recent studies indicate that many alcoholics may not require inpatient treatment. Although there is considerable interest in assigning patients to inpatient or outpatient treatment on the basis of their individual characteristics, reliable methods are not yet available for determining the treatment setting that is most appropriate for a given patient.

Medical, psychological, and psychiatric costs of alcoholism are estimated at \$15 billion a year. A substantial portion of this amount is spent on treatment of the medical consequences of alcoholism. The costs of treatment should be viewed in light of the current \$117 billion in total economic costs for alcoholism and problem drinking. The cost-benefit ratio of alcoholism treatment is favorable, and studies indicate that alcoholism treatment is an effective way of containing costs throughout the health care system.



# Epidemiology

The epidemiology of alcohol-related problems includes the study of patterns and trends in alcohol use and abuse and the examination of the biological, demographic, social, psychological, and genetic factors that influence them. Successful prevention and treatment measures for alcohol abuse and alcoholism must be based on a knowledge and understanding of alcohol epidemiology.

Continued surveillance by such organizations as the National Institute on Alcohol Abuse and Alcoholism (NIAAA), particularly its Alcohol Epidemiologic Data System (AEDS); the National Center for Health Statistics (NCHS); the Centers for Disease Control (CDC); and the National Highway Traffic Safety Administration (NHTSA) provides a broad data base for analysis of patterns and trends in consumption, morbidity, and mortality. In-depth alcohol-related research is performed by scientists of various disciplines throughout the United States. Recent reviews by Lex (1985) and Russell (1986) provide comprehensive bibliographies of alcohol-related epidemiologic research.

This chapter focuses first on patterns and trends in alcohol consumption and on patterns of alcohol-related morbidity and mortality. It also examines the nature and extent of alcohol dependence and alcohol abuse; the role of alcohol in crime; the correlates of alcohol use and abuse in the special population categories of women, adolescents, the elderly, the homeless, and ethnic minority groups; and the overall cost to society of alcohol abuse.

## CONSUMPTION

The amount of alcohol consumed by the entire drinking population is estimated on the basis of alcohol sales in each State. Sales are measured by State reports of tax revenues or of quantities sold in State-controlled stores or by reports from beverage industry sources such as the U.S. Brewers Association and the Distilled Spirits Council of the United States (NIAAA 1985c).

### Per Capita Consumption

Per capita consumption of alcohol is estimated on the basis of total consumption of alcoholic beverages in the United States as determined by sales statistics, divided by the total drinking-age population. Many studies define this as the population 21 years old and older, although some States have not yet raised their minimum drinking age to 21. AEDS bases its per capita consumption estimates on the population 14 years old and older, with the age of 14 years being considered a realistic estimate of the average age at which alcohol use actually begins (NIAAA 1985c). Estimates of per capita consumption using any single age group are thus only approximations of actual drinking levels.

For the entire U.S. population 14 years old and older, the estimated per capita consumption in 1984 was the equivalent of 2.65 gallons of pure alcohol per person

(Williams et al. 1986). This is the amount of alcohol one would obtain from approximately 50 gallons of beer, or 20 gallons of wine, or more than 4 gallons of distilled spirits. When abstainers are excluded and total alcohol consumed is divided by the estimated number of drinkers 14 years old and older, however, estimated actual consumption by drinkers averages approximately 4 gallons of pure alcohol per drinker.

Figure 1, illustrating long-term alcohol consumption trends, shows a sharp rise in apparent consumption following the repeal of Prohibition through the 1940s, followed by a flattening out through the 1950s. After a steady rise through the 1960s and 1970s, the rate of increase slowed and an apparent downward trend began after 1981. The 1984 per capita consumption estimate of 2.65 gallons was the lowest since 1977. This estimate represented the third successive annual decrease in total per capita alcohol consumption and was the first time since Prohibition that consumption declined for 3 consecutive years (Williams et al. 1986).

Consumption of both beer and spirits declined in 1984, although wine consumption increased slightly, continuing a gradual upward trend that began in the 1960s. Beer consumption followed a pattern similar to that for total alcohol consumption, reaching the highest level in 1981

and declining each year thereafter. Consumption of spirits continued a long decline that began in 1970, dropping in 1984 to a new low of 0.94 gallon per person. This represented a 17 percent decrease in apparent annual consumption of spirits from a high of 1.13 gallons per person in 1969.

## Drinking Patterns

Studies of drinking patterns are generally based on self-reports in surveys of the general population. Comparisons among these studies are sometimes hampered by a lack of consistency in defining categories of drinking, although most researchers agree on the definition of abstainers as persons who have not had a drink during the preceding year. Many studies define levels of consumption in terms of ounces per day of pure alcohol (Clark and Midanik 1982; Wilsnack et al. 1984a, b, 1985; Malin et al. 1986). The 1-ounce-per-day level of alcohol consumption that defines heavier drinking by the criteria used in these studies is the approximate equivalent of an average of two drinks per day, whether they are consumed as two cans of beer, two glasses of wine, or two 1.5-ounce drinks of spirits. However, this system of classification averages consumption over a given time period, so that a person who actually consumed two drinks every day each week

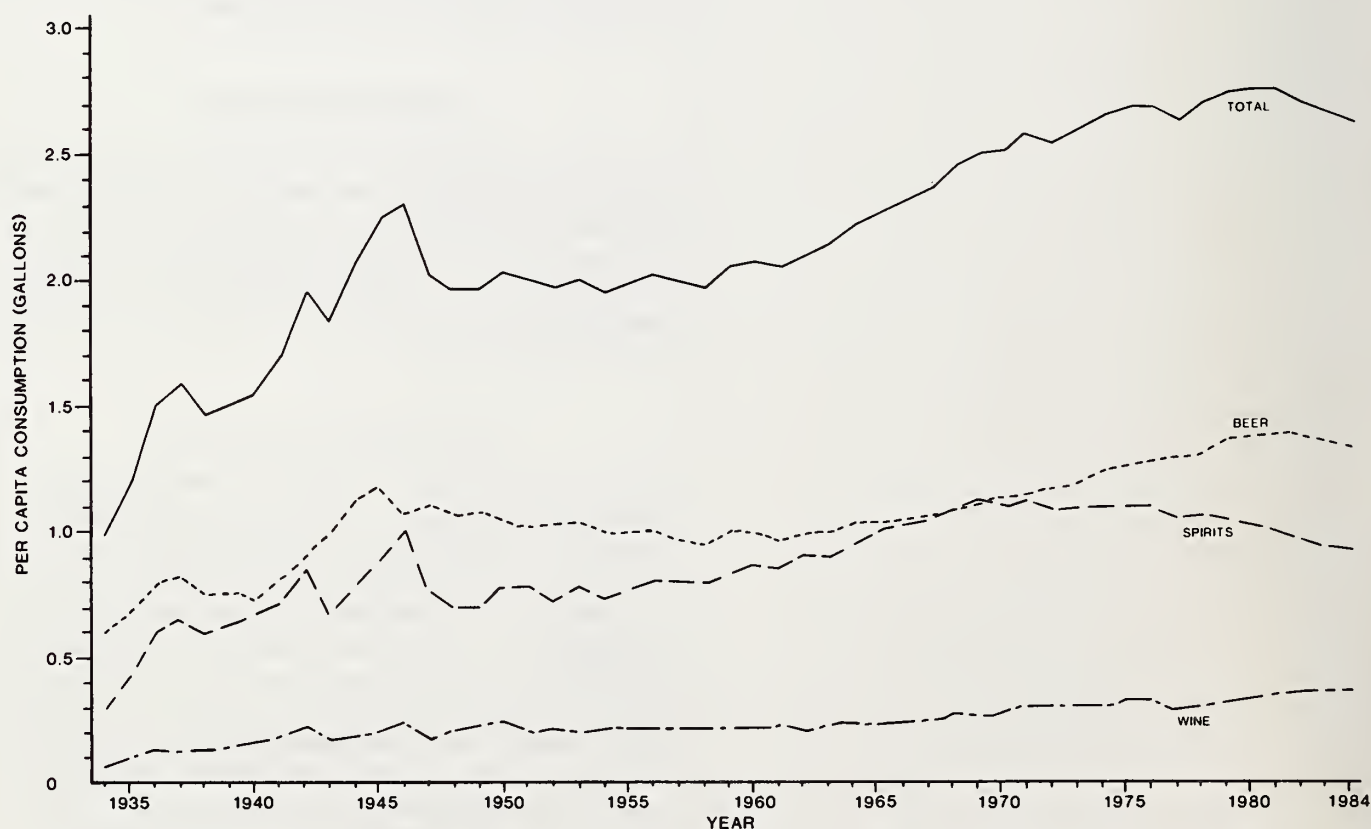


FIGURE 1. Apparent U.S. per capita consumption of alcoholic beverages in gallons of pure alcohol, from the end of Prohibition to 1984.

SOURCES: Data from NIAAA 1985c; Williams et al. 1986.



would be classed with one who consumed, for example, seven drinks a day for 2 days a week and abstained for the other 5 days. These different patterns may have different consequences.

A second set of criteria for defining drinking levels uses a typology that combines amount consumed per occasion (whether or not five drinks are ever consumed at a sitting) with frequency of drinking (never or less than once a year; at least once but less than 12 times a year; from one to three times a month; or at least once a week) (Caetano in press; Herd in press; Hilton in press). According to the definitions used in these studies, frequent heavy drinkers, for example, are defined as those who report having five or more drinks per occasion at least once a week.

National surveys of drinking practices indicate that approximately one-third of the U.S. population ages 18 and over are abstainers, one-third are light drinkers, and one-third are moderate to heavy drinkers (Clark and Midanik 1982; Gallup 1984c; Malin et al. 1986; Hilton in press). In every age group, more men than women are drinkers and, of those who drink, there are more heavy drinkers among men than among women (see figure 2). Among racial and ethnic groups, whites of both sexes are the least likely to be abstainers, whereas relatively high proportions of American Indians and Asian Americans abstain (Malin et al. 1986). Reports of national surveys indicate a recent trend toward increased rates of abstention (Gallup 1984c; NCHS 1985; Malin et al. 1986; Hilton in

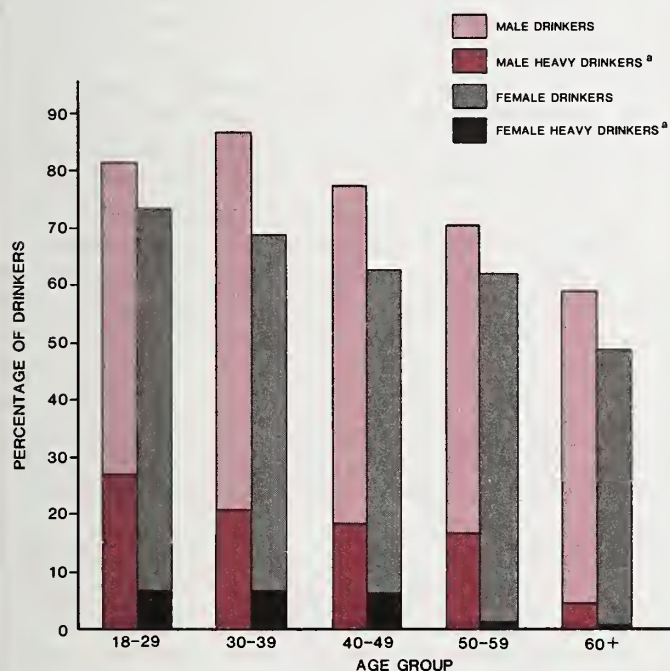


FIGURE 2. Percentage of drinkers by age group and sex, United States, 1984.

SOURCE: Data from Hilton in press.

<sup>a</sup> Those who consume five or more drinks per occasion at least once a week.

press), but preliminary reports from the 1985 National Health Interview Survey indicate little change in the numbers of moderate and heavier drinkers (Thornberry et al. 1986) (see table 1).

Although two-thirds of the adult population drink, actual consumption of alcohol is very unevenly distributed throughout the drinking population. The 10 percent of drinkers (6.5 percent of the total adult population) who drink the most heavily account for fully half of all alcohol consumed, with the other half accounted for by the cumulative 90 percent of the drinking population who are infrequent, light, or moderate drinkers (Malin et al. 1982).

## Geographic Patterns

On a per State basis, apparent 1984 per capita alcohol consumption based on sales statistics ranged from a high of 5.34 gallons in the District of Columbia to a low of 1.53 gallons in Utah (see table 2). However, these figures are only approximations because they do not take into account such variables as sales across State lines, home production, illegal production and importation, or the effects of tourism. For example, apparent per capita consumption in the District of Columbia is influenced by a high level of tourism and by sales to residents of neighboring States.

Per capita alcohol consumption for the adult population in four geographic regions (Northeast, Midwest, South, and West) was estimated for 1983 on the basis of sales statistics and of self-reports of abstention in a national survey of alcohol use (NIAAA 1985c). Consumption in the four regions varied over a fairly narrow range, with apparent consumption levels lowest in the South and highest in the West. However, there were significant regional variations in percentages of drinkers, ranging from 52 percent in the South to 78 percent in the Northeast. When total alcohol consumed was divided by the number of adult drinkers rather than by the total adult population, there was an abrupt shift in relative regional rankings of per capita consumption (see table 3).

TABLE 1. Percentage of population who are moderate or heavier drinkers, by year of survey

Drinking level	1979	1983	1985
<b>Males</b>			
Moderate <sup>a</sup>	31	28	29
Heavier <sup>b</sup>	14	16	14
<b>Females</b>			
Moderate	18	15	15
Heavier	4	4	3
<b>Total</b>			
Moderate	24	21	21
Heavier	9	10	8

SOURCES: Clark and Midanik 1982; Malin et al. 1986; Thornberry et al. 1986.

<sup>a</sup> Moderate drinkers are defined as those who consume an average of 0.22 to 0.99 ounce of pure alcohol per day.

<sup>b</sup> Heavier drinkers are defined as those who consume an average of 1.0 ounce or more of pure alcohol per day.



TABLE 2. *Apparent per capita consumption of alcohol by State, U.S. population ages 14 years old and older, 1980 and 1984*

1984 Rank	State	Per capita consumption (gallons)		1984 Rank	State	Per capita consumption (gallons)	
		1980	1984			1980	1984
1	District of Columbia	5.42	5.34	26	Louisiana	2.71	2.63
2	Nevada	5.82	5.19	27	Oregon	2.82	2.63
3	New Hampshire	5.76	4.91	28	Michigan	2.65	2.60
4	Alaska	3.76	3.86	29	Maine	2.67	2.57
5	California	3.38	3.19	30	North Dakota	2.83	2.55
6	Wisconsin	3.46	3.19	31	Virginia	2.39	2.55
7	Delaware	3.12	3.17	32	South Carolina	2.46	2.50
8	Florida	3.22	3.12	33	Georgia	2.35	2.48
9	Vermont	3.30	3.12	34	Idaho	2.60	2.43
10	Colorado	3.35	3.09	35	Nebraska	2.64	2.41
11	Arizona	3.03	3.08	36	South Dakota	2.56	2.33
12	Massachusetts	3.19	3.04	37	Missouri	2.44	2.27
13	Hawaii	3.31	2.97	38	Ohio	2.33	2.26
14	Montana	3.21	2.95	39	Pennsylvania	2.39	2.25
15	Rhode Island	3.14	2.92	40	Indiana	2.21	2.19
16	Wyoming	3.42	2.86	41	North Carolina	2.17	2.13
17	Maryland	3.09	2.84	42	Iowa	2.25	2.09
18	New Jersey	2.83	2.83	43	Mississippi	2.09	2.06
19	Texas	2.80	2.82	44	Kansas	1.96	1.95
20	Connecticut	2.70	2.80	45	Tennessee	1.92	1.95
21	Illinois	3.00	2.77	46	Oklahoma	1.95	1.91
22	New Mexico	2.99	2.75	47	Alabama	1.86	1.90
23	Washington	3.12	2.71	48	Kentucky	1.91	1.85
24	Minnesota	2.85	2.68	49	Arkansas	1.81	1.78
25	New York	2.91	2.67	50	West Virginia	1.82	1.68
				51	Utah	1.71	1.53

SOURCES: NIAAA 1985c; Williams et al. 1986.

Calculated for drinkers only, apparent per capita consumption over a 13-year period from 1971 to 1983 was consistently highest in the South and lowest in the Northeast. These figures suggest that, although there are more abstainers in the South, persons in the South who do drink tend to be heavier drinkers than persons in the other three geographic regions. Conversely, the Northeast has a relatively high proportion of drinkers, but they consume significantly less per capita than drinkers in the South or West.

When regional differences in consumption were examined in terms of 12 sociodemographic variables, the strongest correlations were found between self-reported drinking levels and urbanization, ancestry, and education of the head of the respondent's household. When urbanization, ancestry, and education were held constant, the regional differences disappeared (Welte and Russell 1982). These results suggest that, at least in the early 1970s, differences in alcohol consumption among geographic regions occurred mainly because of their different sociodemographic compositions.

As noted by Cahalan and Room (1974), the nine U.S. Census regions fall naturally into "wetter" regions (New England, Middle Atlantic, East North Central, Mountain, and Pacific) and "drier" regions (South Atlantic, East South Central, West South Central, and West North Central). Room (1983b) reported that percentages of abstention in the nine regions remained relatively constant over a 15-year period, with the notable exceptions of the Pacific

region, which had a drop in abstention, and the Middle Atlantic and South Atlantic, each of which had an increase in abstention.

Between 1980 and 1984, apparent alcohol consumption either decreased or remained unchanged in 40 States and the District of Columbia (see table 2). In the single year from 1983 to 1984, apparent consumption decreased or remained unchanged in 43 States and the District of Columbia, while only 7 States showed an increase. Most of the increase occurred in the South Atlantic and South Central regions where apparent consumption was the lowest.

TABLE 3. *Apparent alcohol consumption by geographic region for the total U.S. population over age 21 and for the U.S. drinking population over age 21 (excluding abstainers), 1983*

Geographic region	Percentage of adult population over age 21 who drink	Apparent per capita consumption based on total population over age 21 (gallons)	Adjusted apparent per capita consumption based on drinking population over age 21 (gallons)
Northeast	78.1	3.22	5.79
Midwest	72.2	3.00	5.86
South	51.6	2.91	8.01
West	66.0	3.42	7.34
U.S. total	67.0	3.14	6.75

SOURCE: Adapted from NIAAA 1985c.

## ALCOHOL-RELATED MORBIDITY

The types of health problems typically found in heavy drinkers include liver diseases, particularly cirrhosis; diseases of the nervous, gastrointestinal, and respiratory systems; heart and vascular diseases; cancers; metabolic and immune system disorders; endocrine disorders; nutritional deficiencies; poisoning; and injuries from motor vehicle and other accidents (Popham et al. 1984; Ravenholt 1984; Van Natta et al. 1985; NIAAA 1986c). The health effects of maternal drinking on the developing fetus include neurological, behavioral, skeletal, morphological, and developmental disorders, including mental retardation. Fuller discussions of alcohol-related health problems and of fetal alcohol effects are presented in chapters IV and V, respectively.

A study described by Popham et al. (1984) examined the prevalence of diseases, complications, and trauma in a sample of nearly 900 alcoholics admitted to an inpatient treatment program. Among these patients, the highest morbidity rates for men were for fatty liver, chronic obstructive lung disease, and trauma, while the highest rates for women were associated with fatty liver, anemia, and malnutrition.

The National Hospital Discharge Survey (NHDS), conducted by NCHS, provides morbidity data for each year based on discharges from short-stay hospitals (NIAAA 1986c). An examination of data from 1979 to 1984 showed that alcohol-related morbidity was remarkably consistent over the 6-year period, with no strong trends apparent. Alcohol dependence syndrome (a category that includes acute intoxication, other and unspecified alcohol dependence, alcoholic polyneuropathy, alcoholic cardiomyopathy, alcoholic gastritis, and pellagra) accounted for well over half of all alcohol-related diagnoses during this period. The second most prevalent alcohol-related diagnosis was liver cirrhosis, followed by alcoholic psychoses and nondependent abuse of alcohol.

Many nonalcohol-related diagnoses are often associated with alcohol abuse. Approximately 3.1 percent of all discharges for nonalcohol-related disorders between 1979 and 1984 had an alcohol-related diagnosis also present (NIAAA 1986c). The diagnostic category most strongly associated with alcohol-related diagnoses was drug dependence (33.7 percent of cases). Other disorders found in association with alcohol-related diagnoses were, in order of prevalence, diseases of the pancreas; nutritional deficiencies; tuberculosis; neurotic, personality, and other nonpsychotic mental disorders; epilepsy; accidental poisoning; other diseases of the digestive system; diseases of the blood and blood-forming organs; injuries; other metabolic and immunity disorders; diseases of other endocrine glands; pneumonia and influenza; heart failure; malignant neoplasms of the digestive organs and peritoneum; and ischemic heart disease (NIAAA 1986b).

Alcohol consumption, either alone or in combination with smoking, increases the risk of cancer of the gastrointestinal tract, particularly of the mouth, pharynx, larynx, and esophagus (Page and Asire 1985; Cann 1986; Lieber et

al. 1986; McCoy and Napier 1986). It has been estimated that the combined effect of heavy smoking and drinking results in a risk of oral cancer that is more than 15 times as great as for people who neither smoke nor drink (Cann 1986). Liver cancer commonly occurs in association with liver cirrhosis in alcoholics. The prevalence of cirrhosis in patients with liver cancer is generally reported to be between 55 and 80 percent (Lieber et al. 1986). Viral hepatitis, a disorder found more frequently in alcoholics than in nonalcoholics, has also been observed to be associated with liver cancer (Lieber et al. 1986). Both cirrhosis and hepatitis may thus play a role in the pathogenesis of primary liver cancer in alcoholics.

Consumption of tobacco together with alcohol increases the risk of developing cancer above the level of risk from use of either substance alone (Page and Asire 1985; Lieber et al. 1986; McCoy and Napier 1986). Because pure alcohol does not cause cancer in laboratory animals, it is suspected that alcohol may act as a cocarcinogen when used with tobacco. The observed synergistic effect of tobacco and alcohol consumption may be the result of metabolic activation by alcohol of tobacco-associated carcinogens (McCoy and Napier 1986).

## ALCOHOL-RELATED MORTALITY

NCHS maintains data files on all deaths recorded in the United States. For each death, information is recorded on the underlying cause of death as well as on any contributing causes, along with demographic information. Despite the availability of this information, it is difficult to assess accurately the impact of alcohol abuse on mortality, especially in minority groups. One reason is substantial underreporting of alcohol related conditions, particularly as contributing causes of death, on death certificates (Van Natta et al. 1985; Bertolucci et al. 1985b). Only about 3 percent of recorded deaths are officially attributed to causes directly linked to alcohol. This underreporting may be due to reporting bias, to physicians' lack of knowledge of decedents' drinking histories, or both. Furthermore, deaths from motor vehicle and other casualties, homicide, suicide, or other causes that are likely to be associated with acute rather than chronic alcohol abuse are probably seriously underreported.

Van Natta et al. (1985) analyzed NCHS data tapes on the 2 million deaths recorded for a single year, 1978. They found that only 1.9 percent listed an alcohol-related condition as the underlying cause of death, although an additional 1.2 percent of certificates listed an alcohol-related condition along with the specified cause of death. Table 4 lists total mortalities in the United States in 1980 that are attributable to various causes that have been identified as being alcohol related, along with numbers and percentages of those deaths that were attributable to alcohol abuse.

Bertolucci et al. (1985a) calculated the number of years of potential life lost per person due to alcohol for several specific alcohol-related causes of death. Their estimates were based on total numbers of deaths recorded in the United States in 1980 for persons up to the age of 64 years.



TABLE 4. *Estimated number of deaths attributable to alcohol: United States, 1980*

Cause of death	Number of deaths	Estimated number attributable to alcohol	Percentage attributable to alcohol
Alcohol as the main cause			
Alcoholic psychoses	454	454	100
Alcohol dependence syndrome	4,350	4,350	100
Nondependent use of alcohol	889	889	100
Alcoholic polyneuropathy	4	4	100
Alcoholic cardiomyopathy	650	650	100
Alcoholic gastritis	84	84	100
Alcoholic fatty liver	1,166	1,166	100
Acute alcoholic hepatitis	794	794	100
Alcoholic cirrhosis of the liver	9,166	9,166	100
Alcoholic liver damage unspecified	1,812	1,812	100
Accidental poisoning by alcohol	218	218	100
Subtotal		19,587	
Alcohol as a contributing cause			
Cancer of directly exposed tissues			
Malignant neoplasm of lip, oral cavity, pharynx	8,553	2,138	25
Malignant neoplasm of larynx	3,412	853	25
Malignant neoplasm of stomach	14,372	2,874	20
Malignant neoplasm of liver	5,618	1,404	25
Subtotal		7,269	
Other diseases			
Diabetes mellitus	35,649	1,782	5
Hypertensive diseases	32,633	1,632	5
Pneumonia and influenza	54,619	2,731	5
Diseases of esophagus, stomach, duodenum	8,734	873	10
Chronic liver disease and cirrhosis not specified as alcoholic	18,645	4,661	25
Subtotal		11,679	
Accidents			
Railway accidents	632	63	10
Motor vehicle traffic accidents	51,930	25,965	50
Other road vehicle accidents	232	46	20
Water transport accidents	1,429	286	20
Air and space accidents	1,494	149	10
Accidental falls	13,294	3,324	25
Accidents caused by fire and flames	5,822	1,455	25
Accidents due to natural and environmental factors	3,194	799	25
Accidents caused by submersion, suffocation, and foreign bodies	10,216	3,576	35
Other accidents	8,744	2,186	25
Subtotal		37,849	
Violence			
Suicide	26,869	8,061	30
Homicide	23,967	11,984	50
Undetermined whether accidental or purposely inflicted	3,663	1,099	30
Subtotal		21,144	
All causes		97,528	

SOURCE: Ravenholt 1984.

Analysis of mortality data on eight direct or contributing causes of death linked specifically to alcohol showed that death caused by excessive blood alcohol resulted in an average estimated loss of 29.1 years of potential life; death from alcohol abuse, 24.1 years; alcoholic gastritis, 17.8 years; alcoholic psychosis, 15.8 years; alcohol dependence, 15 years; alcoholic cardiomyopathy, 15 years; alcoholic cirrhosis, 14.4 years; and alcoholic polyneuropathy, 5.8 years.

Barr et al. (1984) studied the relative mortality rates of more than 500 alcoholics who either remained abstinent or relapsed after discharge from treatment. Among the 152 who remained abstinent, the mortality rate at 2-year follow-up was not significantly greater than the rate that would be expected for the general population. Excess deaths were found only among those alcoholics who resumed alcohol abuse after treatment. Violent deaths (accidents, homicide, and suicide) were the most excessive.

## Liver Cirrhosis

Liver disease is the main chronic health hazard of alcohol abuse and was the ninth leading cause of death in the United States in 1983, with nearly 28,000 deaths attributed in that year to liver cirrhosis (Grant et al. 1986). However, the proportion of cirrhosis deaths directly attributable to the effects of alcohol abuse cannot be accurately determined. It is very difficult to make pathological differentiations between alcoholic and nonalcoholic liver injury; moreover, some physicians may be reluctant to include mention of alcohol on death certificates because of the stigma associated with alcoholism (NIAAA 1985b). Therefore, mortality data for specified alcohol-related cirrhosis probably do not reflect its true prevalence. However, it is generally agreed that about 50 percent of all cirrhosis deaths are alcohol related, although some estimates are as high as 95 percent (USDHHS 1984).

For the reasons already outlined, the NIAAA's statistical study of liver cirrhosis mortality (NIAAA 1985b) is based on all deaths from cirrhosis, whether or not they are specified as alcohol related. The report analyzes temporal trends in cirrhosis mortality as well as geographic patterns of distribution and correlations of cirrhosis mortality with race, sex, and age.

Cirrhosis mortality rates are significantly higher in non-whites than in whites. In both these racial categories, cirrhosis mortality rates are higher among men than among women, as would be expected from the higher levels of consumption by men of both groups. Race and sex differences in cirrhosis mortality rates are discussed in greater detail later in this chapter.

The geographic distribution of cirrhosis mortality by State for 1980 appeared to be regional, with the States having the highest mortality rates concentrated mainly on the East Coast and among the southern Mountain and Pacific States. In contrast, the lowest cirrhosis mortality rates in that year were found in the Central United States and in the Mountain States of Idaho and Utah. This pattern corresponds broadly to the historic per capita consumption patterns discussed earlier.

Overall cirrhosis mortality in the United States rose through the 1950s and 1960s until it peaked at an age-adjusted death rate of 15.0 per 100,000 population in 1973 (NIAAA 1985b) (see figure 3). The rate has been steadily decreasing since 1973 and, in 1983, was 10.4 per 100,000, the lowest since 1959.

Reasons for the decline are not known. Possible contributing factors are improved medical treatment and successful prevention programs, but any complete explanation should take into account the variations in categories of liver cirrhosis as defined by the International Classification of Diseases (ICD) system. The most recent revision of this system, ICD-9, which took effect in 1978, created many new subdivisions of diagnostic categories, including the separation of alcoholic cirrhosis of the liver into four classes and separation of the two previously specified nonalcohol-related cirrhotic conditions into six conditions (Colliver et al. 1985; Grant et al. 1986).

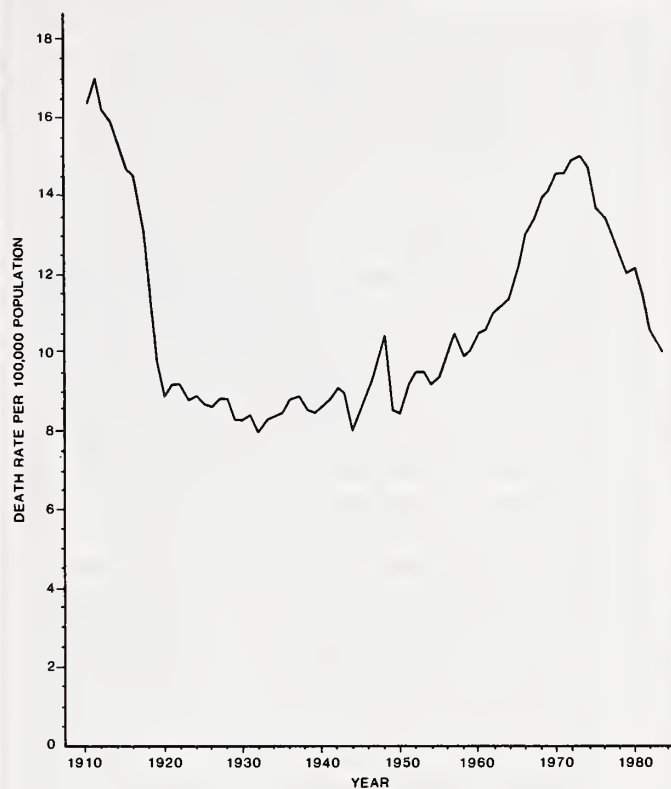


FIGURE 3. Age-adjusted mortality rates from cirrhosis of the liver, United States, 1910-1983.

SOURCE: Data from Grant et al. 1986.

The various classifications of cirrhosis did not contribute equally to the overall decline in liver cirrhosis since 1973. Reductions in alcohol-related and unspecified cirrhosis mortality rates were generally much less than those associated with specified cirrhosis. The relatively rapid decline in mortality in the categories without mention of alcohol may reflect a true decrease in cirrhosis deaths from causes other than alcohol. Conversely, this decline may reflect a greater willingness on the part of physicians to designate cirrhosis deaths as alcohol related. The result would be to accelerate the apparent decline in mortality for nonalcohol-related cirrhosis while decelerating the apparent decline in alcohol-related mortality (Grant et al. 1986).

## Trauma

Use and abuse of alcohol influence the likelihood of almost all types of trauma (Committee on Trauma Research 1985). The high prevalence of injury among heavier drinkers suggests that a history of trauma actually may be useful in the early detection of alcohol abuse (Skinner et al. 1984). Furthermore, alcohol consumption has been shown to increase the risk of serious injury in trauma victims (Luna et al. 1984; Committee on Trauma Research 1985).



## Motor Vehicle Crashes

Motor vehicle crashes are the most common nonnatural cause of death in the United States, accounting for more fatal injuries than any other type of accident (NIAAA 1985a). During 1984, more than 44,000 traffic fatalities occurred on U.S. highways. Forty-two percent of all drivers involved in these crashes were tested for blood alcohol concentration (BAC), but one-fifth of these results were not reported. Thus, the BAC was known for only one-third of all drivers involved in traffic fatalities (NHTSA 1985).

Among fatally injured drivers who were tested for BAC between 1980 and 1984, there was a significant, steady decrease in both numbers and percentages of those who were intoxicated (Fell 1985; NHTSA 1986). The proportion of fatally injured drivers who were legally intoxicated dropped from 50 percent in 1980 to 43 percent in 1984 (see table 5 and figure 4). Although the total number of fatally injured drivers decreased 11 percent from 1980 to 1984, the estimated number of drivers who were intoxicated decreased 24 percent over the same period. Despite a slight increase in total fatalities among drivers between 1983 and 1984, the number of fatalities involving intoxicated drivers decreased.

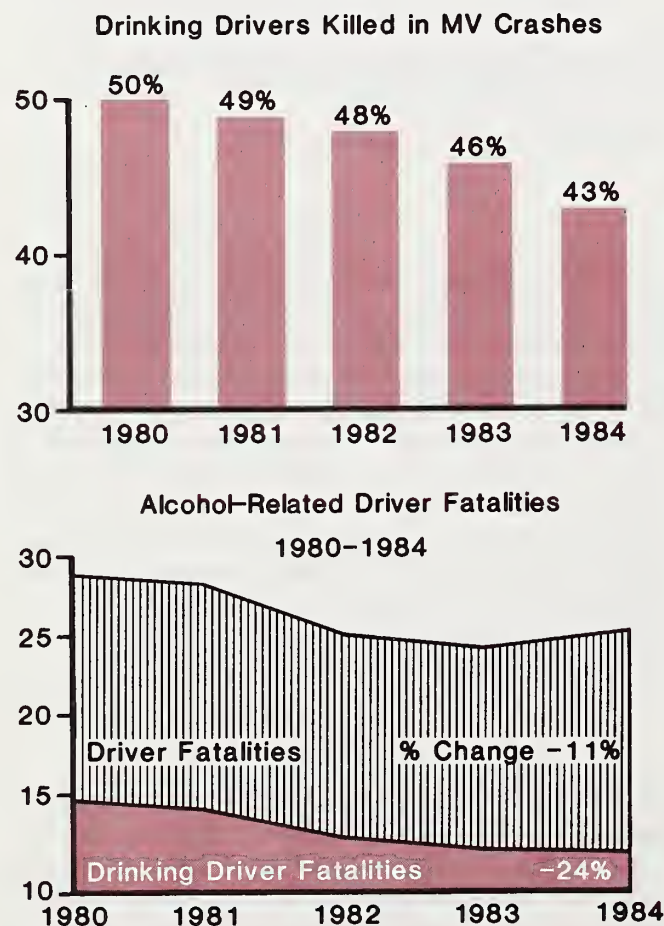


FIGURE 4. Intoxicated drivers (BAC 0.10 percent or higher) killed in motor vehicle crashes, United States, 1980-1984.

SOURCE: NIAAA 1986b.

Data in table 5 are taken from only 15 States, those that have consistently tested blood alcohol in at least 80 to 90 percent of drivers killed in traffic accidents; the results are then projected to the Nation as a whole (Fell and Klein 1986). Several studies by AEDS analyzed traffic fatalities using BAC results from all States rather than limiting data to these 15 selected States (Lowman et al. 1983; Verdugo et al. 1983; Malin and Verdugo 1984; Zobeck et al. 1984; Aitken and Zobeck 1985). Differences in the results reported by NHTSA and AEDS are primarily due to this difference in methodology. Both NHTSA and the AEDS studies considered traffic fatalities to be alcohol related if an involved driver (or pedestrian) had a measurable BAC (0.01 percent or higher) or if the investigating officer judged that the driver (or fatally injured pedestrian) had been drinking. Although most States define legal intoxication as having a BAC of 0.10 percent or higher, alcohol may cause a deterioration of driving skills at 0.05 percent or even lower, and deterioration progresses rapidly with rising BAC (American Medical Association, Council on Scientific Affairs 1986).

According to AEDS criteria, 42 percent of all traffic fatalities (drivers, passengers, pedestrians, and bicyclists) in 1983 were alcohol related. Of the drivers involved in these accidents, 30 percent had a positive BAC or were judged to have been drinking (Zobeck et al. 1984). Although fatalities declined in absolute numbers between 1979 and 1983, the proportion that were alcohol related increased (see table 6).

Fell (1983) analyzed, for 11 age groups, the percentage of all licensed drivers, the percentage of total vehicle miles driven, and the percentage of involvement in alcohol-related fatal accidents in 1980. His results showed that 18-year-olds, who made up only 2.2 percent of the driver population and drove less than 2 percent of total miles traveled, were involved in 5.5 percent of alcohol-related accidents. In contrast, the 45- to 54-year-old age group had six times as many drivers as the 18-year-olds, drove nine times as many miles, yet had only one and a third times as many alcohol-involved fatal accidents.

TABLE 5. Intoxicated drivers (BAC 0.10 percent or higher) killed in motor vehicle crashes, United States, 1980-1984

Year	Total number of fatally injured drivers	Number of fatally injured drivers who were intoxicated	Percentage of fatally injured drivers who were intoxicated
1980	28,816	14,408	50
1981	28,200	13,818	49
1982	24,690	11,851	48
1983	24,138	11,103	46
1984	25,582	11,000	43
Percentage change 1980-1984	- 11%	- 24%	

SOURCE: Fell 1985.

Note: Projections are based on analysis of BACs of fatally injured drivers in 15 States that have consistently tested drivers killed in motor vehicle crashes from 1980 through 1984 (see text).



TABLE 6. *Alcohol-related traffic fatalities (drivers, passengers, pedestrians, and bicyclists), United States, 1979-1983*

Fatalities	Number of fatalities				
	1979	1980	1981	1982	1983
All fatalities	51,084	51,077	49,268	43,721	42,584
Alcohol-related fatalities	20,245	21,114	20,658	18,622	17,847
Percentage alcohol-related	40	41	42	43	42

SOURCE: Aitken and Zobeck 1985.

A special report on male drivers under the age of 25 compared this group with all other drivers in terms of the proportion of intoxicated drivers in different types of accidents and under various conditions (NHTSA 1983). Overall, of young male drivers who were tested after involvement in fatal accidents, 38 percent had a BAC of 0.10 percent or higher, compared with 30 percent for all others in the study. A BAC of 0.10 percent is, in most States, the legal definition of intoxication. However, when the comparison was made according to time of day or day of the week, the percentages of intoxicated drivers were the same or lower for the young drivers (see table 7). The only time when male drivers under the age of 25 had a higher proportion of high BAC levels than all other drivers was during daytime hours on weekends. During weekend nighttime hours, when numbers of intoxicated drivers are the highest, young male drivers involved in fatal accidents showed a substantially lower proportion of high-BAC drivers, with 64 percent at or above the intoxication level, compared with 77 percent for all others.

These figures suggest that the higher overall alcohol involvement of young men may reflect their greater propensity to drive during the high-risk time periods when there is greater use of alcohol. When proportions of all intoxicated drivers involved in fatal accidents were compared across 13 age groups, the percentages were highest (about 37 percent) for those ages 20 to 34 and progressively decreased (to a low of 7 percent) for those over age 69, but these differences tended to even out for accidents occurring in the specific high-risk time period of weekend nights (see table 8).

Studies of the actual BAC level in drivers of five different age groups who were involved in fatal motor vehicle accidents (Verdugo et al. 1983; Malin and Verdugo 1984; Aitken and Zobeck 1985) showed that among 16- to 19-year-olds, the greatest number of fatal accidents occurred at a much lower level of BAC than among persons

TABLE 7. *Percentage of legally intoxicated drivers involved in fatal accidents, by accident condition and driver category, United States, 1980*

Accident conditions	Percentage of drivers with BAC of 0.10 or more		
	Males under 25	All others	All drivers
Single-vehicle	55	55	55
Nighttime	50	50	50
Single-vehicle week-end night	64	77	70
All accidents	38	30	33

SOURCE: NHTSA 1983.

in older age groups. This could indicate that younger drivers are at greater risk of becoming involved in fatal accidents at lower BAC levels because of their relative inexperience in both drinking and driving. It could also indicate that more young drivers are required to take BAC tests and that therefore a greater number of low test scores are recorded for them. However, 62 percent of all tested drivers ages 16 to 19, and 71 percent of those ages 20 to 34, had a measurable BAC (0.01 percent or more), compared with 49 percent of tested drivers over age 34 (Verdugo et al. 1983). Age-group differences cannot be accurately evaluated without uniform administration of BAC tests.

In 1984, fatally injured drivers of certain types of vehicles were more likely to have been using alcohol than were drivers of other types of vehicles (NHTSA 1986). Alcohol was involved in nearly 60 percent of fatal motorcycle accidents but in less than 20 percent of fatal accidents among drivers of heavy trucks. More than 60 percent of fatally injured drivers of light trucks were found to have been drinking, and more than half were legally intoxicated (with BACs of 0.10 percent or higher).

Alcohol use is correlated with a lower rate of safety belt use. Although only 7.2 percent of sober drivers involved in fatal accidents in 1984 were wearing safety belts, a significantly smaller proportion of the drivers who had been drinking (2.2 percent) wore such restraints (NHTSA 1986).

A trauma center study of victims of motorcycle crashes over an 18-month period found a 25 percent incidence of intoxication (Luna et al. 1984). Intoxicated motorcyclists were responsible for the crash 50 percent more often than those who were not intoxicated, and their mortality rate

TABLE 8. *Percentage of legally intoxicated drivers involved in fatal accidents, by age, United States, 1980*

Age group	Percentage of drivers with BAC of 0.10 or more	
	All accidents	Weekend nighttime accidents
Under 16	10	37
16-19	29	56
20-24	37	67
25-29	35	72
30-34	36	80
35-39	31	76
40-44	27	66
45-49	27	71
50-54	22	65
55-59	19	66
60-64	18	73
65-69	16	61
Over 69	7	40

SOURCE: NHTSA 1983.



was four times higher. Although intoxicated motorcyclists constituted only 25 percent of the crash victims, they sustained 39 percent of the severe head injuries and 57 percent of the mortalities. Furthermore, intoxicated motorcyclists wore helmets one-third as often and sustained head injuries twice as frequently.

Alcohol is a significant factor in pedestrian and bicyclist fatalities, as shown by results of blood alcohol test results obtained for 41 percent of such victims (NHTSA 1985). In about 42 percent of the tests, the BAC exceeded the intoxication level of 0.10 percent, and in 23 percent of the tests the BAC was 0.20 percent or higher.

Because blood tests are not routinely administered in fatal crashes in which the driver of the vehicle involved is not killed, the extent of alcohol involvement on the part of the driver in such accidents is not clear. NHTSA estimates that 50 to 55 percent of all fatal motor vehicle accidents involve either a drunk driver (whether the driver is killed or not) or a drunk pedestrian (Fell 1985).

### *Railroad, Aviation, and Boating Accidents*

A study of drinking practices and of the medical and social consequences of drinking among 234,000 railroad employees estimated that 44,000 (19 percent) of the workers were problem drinkers, defined as those whose alcohol use caused harm to themselves or to others (Mannello and Seaman 1979). Between 1975 and 1984, alcohol- or drug-impaired employees were implicated in 48 train accidents/incidents that resulted in 37 deaths, 80 nonfatal injuries, and \$34.2 million in damage (*Federal Register* 1985). Because of the existing latitude in the current reporting system, alcohol and drug involvement in railroad accidents and injuries is very likely to go undetected or unreported in a significant number of cases. Therefore, these figures probably understate the extent of alcohol and drug use on the Nation's railroads (*Federal Register* 1985).

Between 1975 and 1981, the National Transportation Safety Board (NTSB) reported 28,849 aviation accidents in the United States, nearly 5,000 of them (17 percent) involving fatalities (see table 9). A total of 460 accidents, 414 involving fatalities, were found to be alcohol related.

General aviation, which makes up the largest segment of U.S. civil aviation, had the largest number of alcohol-related accidents (440). Of these, 394 were fatal accidents causing 742 deaths.

Of pilots fatally injured in general aviation accidents, 10.5 percent had measurable levels of alcohol in their bodies. In a randomly selected sample of 119 pilots involved in alcohol-related general aviation accidents, about 86 percent had BAC levels of 0.04 percent or higher and 45 percent had BAC levels of more than 0.15 percent (NTSB 1984).

Studies of pilot performance using a flight simulator (Henry et al. 1974) or during actual instrument flight conditions (Billings et al. 1972) showed that performance could be significantly impaired by BACs well below the 0.10 level that is used by most States to define legal intoxication. A level of 0.04 percent has been shown to cause a measurable decrease of attention and skills, and this is exacerbated in aviation by the physiological effects of reduced atmospheric pressure (NTSB 1984).

The Federal Aviation Administration (FAA) prohibits pilots from flying while under the influence of alcohol and has defined 0.04 as the BAC level that constitutes an alcohol-influenced state (*Federal Register* 1986). The NTSB recommends that this level be defined as the lowest BAC measurable with current testing instruments, consistent with the belief that the presence of any alcohol in a pilot's blood jeopardizes safety and is therefore unacceptable.

Boat operators' peripheral vision, balance, and information-processing capability have been shown to be affected almost immediately by alcohol consumption, and the ability to perform boating operations is significantly impaired at a BAC of 0.035 percent (Wyle Laboratories 1975). A 150-pound person could reach this BAC by drinking as little as 18 ounces of beer or 1.5 ounces of whiskey in a 1-hour period (NTSB 1983). In most States, it is unlawful to operate a recreational boat while under the influence of alcohol, but only 11 States have defined the level of intoxication for operators of vessels and most States cannot perform tests without consent (NTSB 1983).

In 1983, the U.S. Coast Guard received reports of 5,569

TABLE 9. *Alcohol involvement in aviation accidents, United States, 1975-1981*

	General aviation							Total general aviation	Total all aviation
	1975	1976	1977	1978	1979	1980	1981		
All accidents	4,006	4,023	4,083	4,218	3,825	3,597	3,502	27,249	28,849
Fatal accidents	636	662	663	721	638	622	654	4,596	4,947
Conclusive toxicological tests <sup>a</sup>	443	462	469	502	455	438	487	3,256	3,536
Positive alcohol tests	48	52	45	52	36	57	53	343	358
Percentage positive	10.9	11.3	9.6	10.4	7.9	13.0	10.9	10.5	10.1
Other known alcohol-related accidents <sup>b</sup>	19	19	24	16	6	4	9	97	102
Total alcohol-related accidents	67	71	69	68	42	61	62	440	460

SOURCE: NTSB 1984.

<sup>a</sup>Toxicological tests are not always possible.

<sup>b</sup>Accidents in which alcohol involvement was determined from witness statements.



recreational boating accidents that resulted in 1,241 fatalities and 2,913 injuries (USCG 1984). However, the Coast Guard estimates that it receives reports of only 5 to 10 percent of all reportable accidents that do not involve fatalities (USCG 1984).

Recent studies by several States (California, Maryland, and North Carolina) (NTSB 1983) indicate that the full extent of alcohol involvement in recreational boating accidents, injuries, and fatalities appears to be grossly underreported. Although available Coast Guard data for 1982 indicated that less than 2 percent of accidents and only 6 percent of fatalities involved alcohol, the State studies showed that 75 to 80 percent of boating accidents and deaths were alcohol related and, in 35 to 38 percent of these fatalities, the victims were legally drunk (with BACs of 0.10 percent or higher) (NTSB 1983). These data, together with information from various other sources, suggest that from one-third to two-thirds of boating fatalities may be alcohol related (NTSB 1983).

### *Drownings, Fires, and Falls*

Drowning is the third leading cause of accidental death in the United States, with alcohol involved in an estimated 69 percent of drowning deaths (NTSB 1983). Of the 1,241 boating deaths recorded in 1983, 1,096 (88 percent) were the result of drowning (USCG 1984). Research has shown that a person under the influence of alcohol is much more susceptible to drowning than is a person who is sober, because of disorientation, exacerbated thermal responses to water temperature, and impairment of psychomotor skills and breath-holding time (NTSB 1983).

In Canada, drowning is the second leading cause of accidental death among persons under 20 years of age, with males between the ages of 15 and 19 at particular risk (MacLachlan 1984). An investigation of 263 drowning fatalities between 1979 and 1981 found that 41 of the victims (16 percent) had measurable alcohol or drug levels, and 38 of these 41 victims (93 percent) were 15- to 19-year-old males. In New Zealand, Cairns et al. (1984) performed an autopsy study on 225 drowning victims over the age of 15. A total of 150 (129 males and 21 females) drowned accidentally, while 60 (31 males and 29 females) committed suicide by drowning. Of the 97 victims for whom BAC estimations were available, nearly half had detectable levels of alcohol and 36 (29 males and 7 females) were legally intoxicated (with BACs of 0.10 percent or higher). Although both of these studies found measurable quantities of blood alcohol in a substantial proportion of drowning victims, they do not allow assessment of the contribution of alcohol consumption to increased risk of drowning. This is because blood alcohol concentrations were not measured in the entire population who were at risk of drowning, i.e., all the people who were at the beach or the swimming pool and, drinking or not, actually went into the water during the periods when the drownings occurred. In other words, these studies lack a comparison of drowning rates between those who had measurable blood alcohol levels and those who did not.

A review of the medical records of 70 burn patients over the age of 14 found that 46 percent had been using alcohol, either alone or with an illicit drug, at the time of injury (Vogtsberger and Taylor 1984). Most of the burns occurred in the home (57 percent) or near vehicles (27 percent). Most of the male burn patients (58 percent) had been drinking at the time of injury, compared with 26 percent of the female patients, and most of the males (53 percent) were between 15 and 26 years old, while nearly half the women were over the age of 35. In 18 percent of the patients, pathological patterns of alcohol use warranted psychiatric diagnoses of alcohol abuse or alcohol dependence.

A study of 283 violent deaths among alcoholics found that 7 were attributable to fires (Combs-Orme et al. 1983). This figure represents 2.4 percent of all the deaths and is 26 times the expected rate. Two of the seven deaths were attributed to careless smoking, an area in which there has been little recent research. There is clearly a need for studies of the combined effects of drinking and smoking, both in causing fires and in impairing escape from them.

Falls are a major cause of trauma. A study of 313 emergency room patients who had suffered accidental falls found that 60 percent had detectable levels of alcohol in their blood and 53 percent of these fall victims had BACs above 0.2 percent (Honkanen et al. 1983). Risk estimates in this study showed a steep rise in relative risk of accidental fall with increasing BAC. With relative risk set at 1 for zero BAC, the risk was about 3 for BACs of 0.05 to 0.10 percent, 10 for BACs of 0.10 to 0.15 percent, and about 60 for BACs of 0.16 percent and higher. It was thus concluded that practically all fall injuries to persons with BACs above 0.10 percent could be considered to have been caused by alcohol.

### *Suicide*

Suicide is among the 10 leading causes of death in the United States for persons 34 to 54 years of age and, with homicide and accidental death, is one of the 3 leading causes of death among males 15 to 34 years old (Abel and Zeidenberg 1985). A recent analysis of 3,400 violence-related deaths in which the victims' BACs were tested found that suicide was the cause of 21 percent of those deaths (Abel and Zeidenberg 1985). In 35 percent of suicides, the victims had been drinking, and intoxication was present at the time of death in 23 percent. These figures are similar to those obtained in earlier studies (Roizen 1982; USDHHS 1984).

Alcoholics have a very high suicide rate as shown by followup studies of alcoholics and by retrospective studies of suicides. A review of several followup studies revealed suicide rates of 8 percent to 21 percent among alcoholics (Kendall 1983). Berglund (1984), in a followup study of 1,300 alcoholics who had been admitted to the psychiatric section of a Swedish hospital over a 20-year period, found a 16 percent suicide rate among the 537 deaths in this group.

A retrospective study (Kendall 1983) suggested that alcoholics who take their own lives tend to be middle-aged and to have been drinking heavily for 20 to 25 years.



However, recent studies indicate that rates for older males have declined, whereas those for persons 15 to 24 years of age have increased (Colliver and Malin 1986).

A Scottish hospital that treats large numbers of patients who have survived unsuccessful suicide attempts found that 50 percent of male suicide attempters had a drinking problem, with 25 percent of them classed as alcohol dependent (Kendall 1983). The proportion of female suicide attempters with drinking problems was lower (23 percent in 1980) but increasing steadily. The contribution of alcohol to suicidal behavior was not limited to alcoholics and problem drinkers in this study; in 1979, 74 percent of the male suicide attempters and 51 percent of the female suicide attempters had been drinking shortly before the attempt. Other studies showed that in 20 to 37 percent of suicides the victim either was drinking or had a history of alcohol abuse (Roizen 1982; Colliver and Malin 1986).

## PREVALENCE OF DRINKING PROBLEMS IN THE UNITED STATES

An estimated 18 million adults 18 years old and older currently experience problems as a result of alcohol use (Williams et al. in press). These problems may include symptoms of alcohol dependence such as loss of memory, inability to stop drinking until intoxication, inability to cut down on drinking, binge drinking, and withdrawal symptoms. Persons with dependence symptoms are defined as alcoholics by the NIAAA. In addition, alcohol abusers are defined as those who, while not showing dependence symptoms, experience negative social or personal consequences of alcohol use, such as arrest, accident involvement, health problems, impairment of job performance, or difficulties in personal relationships. Adolescent alcohol abusers may experience such negative consequences as poor school performance, trouble with parents, or involvement with law enforcement personnel.

Large-scale national surveys have included extensive self-reports of problems associated with drinking in an attempt to assess the prevalence of dependence symptoms and the nature and magnitude of problem consequences of drinking (Clark and Midanik 1982; Wilsnack et al. 1985; Hilton in press; Malin et al. 1986). However, comparisons are hampered by differences in criteria for problem levels, in wording of survey questions, and in interpretation of data.

Clark and Midanik (1982), who compared the prevalence of drinking problems reported in the 1979 national survey with those reported in 1967 (Cahalan 1970), found no clear trends in problem rates over this 12-year period. Analysis of 1984 survey data indicated that approximately 5 percent of all adults surveyed experienced moderate levels of dependence symptoms and 7 percent experienced moderate levels of tangible social or personal consequences associated with alcohol abuse (Hilton in press). Calculated on the basis of drinkers only, excluding abstainers, these figures were 7 percent and 10 percent, respectively. As expected, a higher proportion of men than of women experienced problems, with 14 percent of male and 6 percent of female drinkers reporting a moderate level of

tangible consequences (Hilton in press). A preliminary analysis of data from the Alcohol Health Practices Supplement to the 1983 Health Interview Survey reported similar findings, with 16 percent of male and 6 percent of female drinkers reporting personal problems associated with alcohol use (Malin et al. 1986).

A survey that focused on women's drinking patterns and problems (Wilsnack et al. 1985) confirmed that women had fewer drinking-related problems and fewer dependence symptoms than men. However, this study found that women had higher levels of problem consequences when only the highest level of consumption was considered (those at the upper end of the heavier-drinking category who consumed 2 or more ounces of alcohol per day, the equivalent of four or more drinks). At this level of consumption, 73 percent of women reported two or more problem consequences, compared with 63 percent of men. Women did not, however, exceed men in dependence symptoms at any level of consumption. Of those women who consumed 2 or more ounces per day, 75 percent reported at least one dependence symptom, while 87 percent of men at that consumption level reported one or more such symptoms.

A comparison of problem rates among blacks and whites revealed that, for every type of problem surveyed except drunk driving, black men reported higher rates of problems than white men (Herd in press). More than twice as many blacks as whites reported binge drinking and health problems, but more than two and a half times as many white men as black men reported driving while drunk. Conversely, black women consistently reported fewer alcohol-related problems than white women. The most striking contrast was in drunk driving, with white women reporting driving while drunk more than five times as often as black women. Blacks in the youngest age group (18-29) were at the lowest risk for experiencing drinking problems, while whites of this age were at the highest risk.

About 18 percent of Hispanic men and 6 percent of Hispanic women reported experiencing one or more alcohol-related problems in the year before being surveyed (Caetano in press). Those in the youngest age group (18-29) were at the highest risk, with 22 percent of men and 10 percent of women reporting at least one problem. Of those reporting four or more problems, women in the youngest age group were again at highest risk, but the highest rate among Hispanic men was for those in the 50-59 age group.

The National Institute of Mental Health (NIMH) Epidemiologic Catchment Area (ECA) program is a research study still in progress that is assessing the prevalence and incidence of psychiatric disorders among adults in five geographic locations (Locke and Regier 1986). Preliminary reports from three of these locations (New Haven, Conn.; Baltimore, Md.; and St. Louis, Mo.) indicated that alcohol abuse or dependence was one of the most common disorders found (Myers et al. 1984). The most common diagnoses for women were phobias and major depression, whereas for men alcohol abuse or dependence was by far the most common diagnosis.



Age distributions of disorders by sex were generally similar, with alcohol abuse or dependence predominating in men of all age groups through the age of 64. Among men over 64 years of age, however, it was the third most prevalent diagnosis, exceeded by cognitive impairment and phobia. Among women, alcohol abuse or dependence was one of the four most frequent psychiatric disorders only in the youngest age group, those under the age of 25 years. The 6-month prevalence rates for alcohol abuse or dependence were found to be 4.8, 5.7, and 4.5 percent, respectively, for New Haven, Baltimore, and St. Louis (Myers et al. 1984).

During 1983, an estimated 8 million persons were admitted to local jails throughout the United States (USDOJ 1985). An interview survey of nearly 6,000 jail inmates, designed to provide a representative sample of the Nation's prison population, found that nearly half the convicted inmates had been under the influence of alcohol at the time of the criminal offense for which they were convicted (USDOJ 1985). Of those who had been drinking, more than half admitted that they had been drunk at the time of the offense and 44 percent had been drinking for 5 or more hours.

A comparison of alcohol involvement in relation to the type of crime committed (see table 10) showed that 64 percent of inmates convicted of public-order offenses had used alcohol just before the offense. Public-order offenses include driving while intoxicated, but even with this offense excluded, 45 percent of the public-order offenders had used alcohol. Of offenders convicted of violent crimes, more than half (54 percent) had used alcohol just before the offense. Alcohol involvement was particularly prevalent in cases of manslaughter (68 percent) and assault (62 percent). There was somewhat less alcohol involvement in cases of property crime (40 percent), and drug offenses had the least alcohol involvement (29 percent). Even in the category of lowest alcohol involvement (fraud/forgery/embezzlement), 22 percent of convicted offenders reported alcohol use just before the offense.

A study of alcohol and property crime suggested an opposite cause-and-effect relationship depending on whether the crime was casual or professional (Cordilia 1985). Alcohol use at the time of the offense is a deterrent to involvement in professional property crime, although alcoholism may develop in response to the professional criminal lifestyle (Cordilia 1985). But people who commit crime that is relatively unplanned and unskilled and for whom crime is not a primary occupation are more likely to drink heavily before the crime, often as part of a group.

Studies investigating the relationship between alcohol and homicide have shown that about half of offenders and victims were drinking at the time of the crime (Combs-Orme et al. 1983). Abel and Zeidenberg (1985) found that 45 percent of homicide victims had been drinking and 33 percent were intoxicated (with BACs of 0.10 percent or higher). Analysis of BACs in 4,000 homicide victims in Los Angeles gave very similar results, with 46 percent of victims having measurable BACs and 30 percent legally intoxicated (Goodman et al. 1986; Loya et al. 1986). Male

victims were twice as likely as females to have been drinking, and victims were more likely to be intoxicated in homicides involving a friend, acquaintance, or spouse.

Studies of victims of violent crime show that in cases of robbery, rape, assault, and homicide the offender is more likely to have been drinking if the victim has been drinking and vice versa (Room 1983a). This association is particularly strong for cases of homicide and rape that involve acquaintances and friends. For these offenses and for assaults, the offender and the victim are equally likely to have been drinking. In cases of robbery and rape involving strangers, the victim is more likely than the offender to have been drinking.

The age and sex distributions of criminal behavior in the population are similar to that of heavy alcohol consumption. Men drink more heavily than women, and men account for 80 to 90 percent of those arrested and convicted for serious crimes; also, serious crime peaks in the young

TABLE 10. *Alcohol use among convicted offenders just before committing current offense, by crime type, United States, 1983*

Current offense	Number convicted	Percentage of convicted persons who used alcohol
<i>Total</i>	<i>132,620</i>	<i>48%</i>
<i>Violent</i>	<i>32,112</i>	<i>54</i>
Murder/attempted murder	3,345	49
Manslaughter	1,188	68
Rape/sexual assault	4,017	52
Robbery	11,945	48
Assault	9,609	62
Other violent <sup>a</sup>	2,008	49
<i>Property</i>	<i>51,660</i>	<i>40</i>
Burglary	17,335	44
Auto theft	2,960	51
Fraud/forgery/embezzlement	5,976	22
Larceny	18,001	37
Stolen property	3,676	45
Other property <sup>b</sup>	3,712	51
<i>Drugs</i>	<i>13,181</i>	<i>29</i>
Traffic	5,469	26
Possession	6,830	30
Other drugs	882	44
<i>Public order</i>	<i>34,036</i>	<i>64</i>
Weapons	2,769	32
Obstructing justice	6,856	43
Traffic	3,734	36
Driving while intoxicated <sup>c</sup>	13,406	93
Drunkenness/morals offenses <sup>d</sup>	4,894	70
Other public order <sup>e</sup>	2,377	28
<i>Other<sup>f</sup></i>	<i>1,008</i>	<i>40</i>
<i>Information unavailable</i>	<i>623</i>	<i>—</i>

SOURCE: USDOJ 1985.

<sup>a</sup>Includes kidnapping, purse snatching, hit-and-run driving, and child abuse.

<sup>b</sup>Includes arson, destruction of property, property damage from hit-and-run driving, and trespass.

<sup>c</sup>Includes driving while intoxicated and driving under the influence of drugs.

<sup>d</sup>Also includes vagrancy and commercialized vice.

<sup>e</sup>Includes rioting, habitual offender, family-related offenses such as nonsupport or abandonment, invasion of privacy, and contributing to the delinquency of a minor.

<sup>f</sup>Includes juvenile offenses and unspecified offenses.



adult years when heavy alcohol consumption is the most prevalent (Room 1983a). Moreover, it has been noted that prison populations have a high incidence of drinking problems and, conversely, that alcoholics and problem drinkers are more likely to engage in criminal behavior than are people in the general population. Thus, there is an apparent positive correlation between alcohol use and crime, although the existence and nature of any direct causal relationship are not clear.

## SPECIAL POPULATIONS

### Women

Because of the low rates of heavy drinking among women compared with the rates among men, most surveys of drinking patterns and problems have included relatively little information on women who have high consumption levels and high levels of alcohol-related problems. A national survey was conducted in 1981 to overcome these limitations by oversampling women who drank moderately to heavily or who had histories of drinking-related problems. Results of this survey provide a more accurate and detailed picture of women's drinking patterns and problems (Wilsnack et al. 1984a, b, 1985).

A comparison of results from this survey with the results of eight surveys conducted in the 1970s revealed no evidence of a major increase in alcohol consumption by women over the 10-year period. Women remained predominantly abstainers (39 percent) or light drinkers (38 percent), with increasing abstinence after the age of 50. One change from patterns of the 1970s was an apparent increase in alcohol consumption among middle-aged women (ages 35 to 64), with more drinkers and more heavier drinkers in this age group than were found in the earlier surveys. Contrary to expectations, there was no increase in drinking or in heavier drinking in the youngest age group (ages 21 to 34). A pattern of increased heavy drinking in the middle years (ages 35 to 64) was also found by Fillmore (1985) in a cross-sectional study of drinking patterns among 10-year birth cohorts.

Wilsnack's 1981 survey found that women of lower educational or economic status were more likely to be abstainers. Half the women with household incomes under \$10,000 were abstainers, as were 68 percent of women with no more than an eighth-grade education, compared with 39 percent for all women surveyed. However, low-income

women who did drink were more likely to drink heavily or to drink to intoxication.

Comparisons of women's drinking levels by marital status indicated that women who were divorced or separated or who had never married were relatively unlikely to be abstainers and were relatively likely to be heavier drinkers, whereas most widows were abstainers and very few were heavier drinkers. However, these patterns can largely be accounted for by age differences.

Married women with paid employment outside the home were found to be somewhat less likely than full-time homemakers to be heavier drinkers. However, moderate drinking was more common among married women who worked, particularly among those with part-time jobs, as shown in table 11. Among women with full-time employment who had never married, 49 percent were moderate or heavier drinkers, significantly more than any of the women in the married categories. Similarly, 41 percent of the women who were divorced or separated and were employed full time were moderate or heavier drinkers.

Women's drinking patterns and consequences were strongly associated with the drinking behavior of significant others. There was a close relationship between women's drinking behavior and the number of significant others such as husbands, siblings, and close friends whom they perceived as frequent drinkers. Women with husbands or partners whom they described as frequent drinkers were more likely to report heavier drinking, drinking-related problems, or symptoms of alcohol dependence. However, the women who described their husbands or partners as problem drinkers rather than frequent drinkers were actually less likely to report problems or dependence symptoms of their own.

Although researchers have acknowledged a strong association between domestic violence and high levels of alcohol consumption, the nature of the relationship is not clear. One reason is that battered women, although they make frequent use of emergency room services, are often not identified as battered. In a study by Russell (1982), there was a high rate of problem drinking among battering husbands, especially among those married to women who specifically identified themselves as battered. In 63 percent of these cases, the women reported that their husbands were sometimes, usually, or always drinking when they were violent.

A study of wife rape found that in 20 to 25 percent of cases the husband was drinking at the time of the rape

TABLE 11. *Drinking levels by marital and employment status for women and men (weighted percent)*

Drinking level	All women		Married women			All men	
	Employed full time (N = 361)	Employed part time (N = 135)	Employed full time (N = 189)	Employed part time (N = 97)	Full-time homemaker (N = 177)	Employed full time (N = 265)	Employed part time (N = 28)
Abstainers	32	31	41	34	43	22	33
Light drinkers	40	38	40	37	42	28	14
Moderate drinkers	21	26	14	24	9	36	17
Heavier drinkers	7	4	4	4	6	14	35

SOURCE: Data from Wilsnack et al. 1985.



(Russell 1982). However, these respondents were not asked specifically about alcohol involvement, and it was thought that alcohol consumption in these cases was thus greatly underestimated.

A survey of 1,000 battered wives found that those who used the police as a source of help were more likely than the other battered women to report that their husbands always or usually had been drinking at the time of the battering (Bowker 1984). They further reported that drinking was always or usually the major reason for the violent behavior.

The 1981 survey was the first study to obtain detailed data on drinking and reproductive dysfunction from a representative national sample of women (Wilsnack et al. 1984a). Dysmenorrhea, heavy menstrual flow, and premenstrual discomfort were found to increase with drinking level. There was a particularly strong association of such disorders with at least one 3-ounce (six-drink) drinking episode per week. Women who averaged 1.5 ounces or more of ethanol per day, or who experienced at least five 3-ounce drinking episodes per week, had higher rates of most types of gynecologic surgery. A history of miscarriage or stillbirth, premature birth, birth defects, and infertility was found to be associated with the highest levels of alcohol consumption.

Other studies that controlled for potentially confounding variables, including smoking, confirmed a strong association between fetal mortality and drinking during pregnancy (Harlap and Shiono 1980; Kline et al. 1980; Prager et al. 1984). Harlap and Shiono (1980) also determined that drinking and smoking were independent risk factors for spontaneous abortion, with the effect of drinking greater than that of smoking. Prager et al. (1984) further showed that smoking and drinking were independently and additively associated with low birth weight. The associations between alcohol and reproductive dysfunction and between alcohol and adverse pregnancy outcome, particularly with respect to the fetal alcohol syndrome (FAS), are discussed in greater detail in chapters IV and V.

## Adolescents

Since 1975, the National Institute on Drug Abuse (NIDA) has conducted an annual nationwide survey of about 17,000 high school seniors on the use of drugs, tobacco, and alcohol. The 1984 survey found that reported use of alcohol, as well as of nearly all illicit drugs (particularly marijuana), had declined since 1980 (Johnston et al. 1985). However, the 1985 survey (Johnston et al. 1986) revealed that this declining trend had leveled off for most drugs and that use of cocaine had in fact increased. Despite this halt in the decline of drug use, alcohol consumption continued a steady, though gradual, decline.

In 1985, nearly 5 percent of high school seniors drank every day, fewer than the 1979 high of 7 percent but still representing daily alcohol use by 1 in 20 students. Episodes of heavy drinking (five or more drinks at a time) during the preceding 2 weeks were reported by 37 percent of the seniors, a significant drop from the 1983 level of 41 percent and the lowest level since 1975.

Despite the decline in alcohol use between 1980 and 1985, the proportion of users remained high. Most high school seniors in 1985 (92 percent) reported having used alcohol at least once. More than half of the seniors (56 percent) reported that their first use of alcohol occurred before the 10th grade, nearly 10 percent of them as early as the 6th grade. During the year preceding the 1985 survey, only 14 percent did not use any alcohol. Two-thirds of the seniors had used alcohol during the preceding month, and 20 percent reported drinking during the preceding year but not during the preceding month. Nearly one-third of the seniors (30 percent) said that most or all of their friends got drunk at least once a week; only 18 percent stated that none of their friends got drunk at least once a week.

Frequent and heavy drinking were more prevalent among male students, with more than twice as many males as females drinking daily and nearly half the male students (45 percent) reporting heavy drinking in the preceding 2 weeks compared with 28 percent of the female students. Both percentages represent decreases from the respective 1984 levels of 48 and 30 percent.

A national poll by the Gallup Organization found that, in 1984, 59 percent of adolescents 13 to 18 years old were at least occasional consumers of alcohol and an additional 17 percent had tried alcohol at least once (Gallup 1984b). Two-thirds of those polled had used alcohol before their 16th birthdays. A large majority (83 percent) had friends who were regular users of alcohol (Gallup 1984a). One-third of all those interviewed and more than half of those over age 16 said that all or most of their friends were regular drinkers.

Followup surveys of students 1, 2, and 3 years after graduation from high school examined the interrelated effects of education, occupation, and living arrangements on drug and alcohol use (Johnston et al. 1985). Education and occupation per se had little impact, but clear trends were associated with living arrangements. Alcohol use decreased among those who were married and living with a spouse, remained relatively unchanged among those living with parents, and increased among those living alone or with others in apartments, dormitories, or military quarters.

The 1985 survey included followup studies of graduates who were 1 to 4 years past high school, with a specific focus on college students (Johnston et al. 1986). Patterns of alcohol use among the college students did not vary substantially from use among nonstudents in that age group except for the frequency of occasional heavy drinking (five or more drinks at a time during the preceding 2 weeks). Among the college students, 45 percent drank at this level, compared with 41 percent for the group as a whole and 37 percent for high school seniors. However, the college students reported slightly lower rates of daily drinking (5 percent) than was true for their age group as a whole (6 percent).

When seniors in the 1985 survey were questioned about their perceptions of the degree of risk associated with various levels of alcohol use, 24 percent reported that they perceived a great risk in consumption of one or two drinks

nearly every day; 43 percent believed that there was a great risk in occasional heavy drinking (five or more drinks at a time once or twice each weekend); and 70 percent perceived a great risk in consumption of four or five drinks nearly every day (Johnston et al. 1986). However, 10 years earlier, these figures were, respectively, 22, 38, and 64 percent (see figure 5). Thus, although the data suggest a liberal attitude toward the use of alcohol, they also appear to reflect an increasing awareness of the risks of heavy alcohol consumption.

### The Elderly

According to the U.S. Bureau of the Census, in 1983 there were nearly 26 million persons in the United States age 65 years old or older, more than 11 percent of the population. It is estimated that, by the year 2000, 12.2

percent of the population will be 65 years old or older, and by the year 2025 that figure will rise to 17.2 percent (Williams 1984).

Alcohol abuse is less prevalent among the elderly than among younger age groups (see figure 2). However, estimates of the prevalence of alcohol-related problems in the older age groups vary considerably. Holzer et al. (1984) found that rates of alcohol abuse exceeded 10 percent among men under age 40, but were less than 5 percent among men over age 60 and less than 1 percent in older women. Preliminary data from an epidemiologic study of mental disorders by NIMH indicate that, although alcohol abuse and dependence constitute the most common psychiatric disorder for men and the fifth most common disorder for women, people over the age of 65 have the lowest rates of abuse for both sexes (Robins 1984).

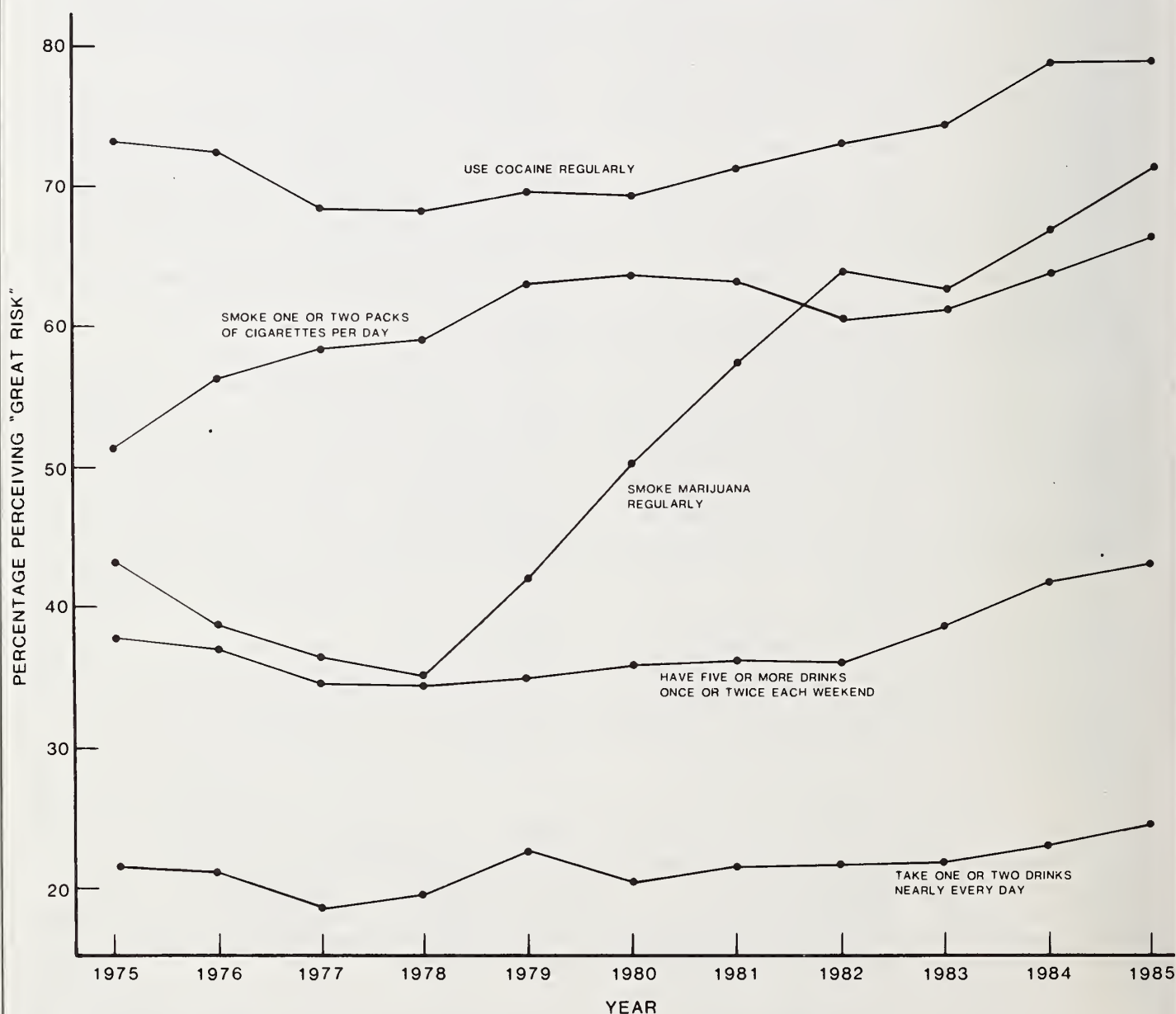


FIGURE 5. Perceived harmfulness of drugs as reported by high school seniors, United States, 1985.

SOURCE: Johnston et al. 1986.



The reasons for the lower prevalence of alcohol abuse in the elderly are not clear. The statistics could reflect actual drops in individual consumption, underreporting of consumption, early death from problems caused by heavy alcohol use, or a combination of these factors. A recent study that followed a population of more than 1,500 men 28 to 84 years old for a 9-year period showed no drop in individual consumption with increasing age (Glynn et al. 1984).

The relatively low prevalence of alcohol abuse among older persons may be due to the reduced tolerance to alcohol that is associated with aging. The biological aging process includes many changes that can influence the body's response to alcohol (Straus 1984). The proportion of body fat increases, while the volume of body water decreases. Because alcohol is distributed in body water, a given amount of alcohol per unit of body weight will produce a higher blood alcohol concentration in an older person. Changes in hormone levels; in rates of absorption, metabolism, and elimination; and in tissue sensitivity also act to decrease the quantity of alcohol that an older person can consume without adverse effects.

Decreases in individual consumption may also be related to an increase in adverse health effects. About one-fourth of the people in this country over age 65 take prescribed medications (Williams 1984), and the interactions of these drugs with alcohol may pose particularly significant health risks.

There are two significantly different types of elderly problem drinkers: those who begin to abuse alcohol earlier in life and continue into old age and those who do not develop alcohol-related problems until their later years (Holzer et al. 1984; Williams 1984). The early-onset drinkers account for about two-thirds of the elderly problem-drinking population. Their long-term alcohol abuse often results in severe medical problems, particularly degenerative diseases of the liver, brain, heart, intestinal tract, and pancreas. Fewer than one-third of elderly problem drinkers are late-onset drinkers who usually begin problem drinking in response to such major late-life stresses as the death of a spouse or other person close to them, retirement, reduced income, poor health, or geographic relocation.

A possible third group of elderly alcoholics has recently been suggested, consisting of people with a history of light or moderate drinking interspersed with occasional binge episodes (Williams 1984). These so-called intermittent drinkers may respond to late-life depression, loneliness, and anxiety with frequent periods of heavy drinking.

## The Homeless

It is not possible to determine accurately the size of the homeless population, but, according to estimates by the U.S. Department of Housing and Urban Development, there are roughly 250,000 to 350,000 homeless persons in the United States and their numbers are increasing (USGAO 1985). Although the homeless traditionally have been viewed as mostly alcoholics, drug addicts, and transients, this subpopulation now includes increasing propor-

tions of the elderly, women, children, minorities, the unemployed, displaced families, and the mentally ill. Many interrelated factors contribute to the increasing numbers of homeless persons, but alcohol abuse remains among the most important (USGAO 1985).

Recent surveys in eight U.S. cities found estimates of alcohol abuse among the homeless ranging from less than 20 percent to 45 percent (Mulkern and Spence 1984). These studies focused mainly on shelter users and on men, although the two studies that did include significant numbers of women found overall problem drinking rates of 25 percent and 32 percent. Although interpretation of these investigations was hampered by inadequate sampling and by the lack of uniform methodology, it is clear that a significant proportion of the homeless are alcohol abusers.

A comparison of homeless alcoholic women at a New York City shelter with alcoholic women interviewed at treatment agencies found that the homeless women were heavier drinkers, were somewhat older (average age 46 years versus 41 years for agency-treated women), and were less likely to be married (Corrigan and Anderson 1984). A higher proportion of the homeless women were black (39 percent, compared with 21 percent of the agency-treated women).

A demographic study of 1,000 homeless persons in Ohio found that 21 percent were self-reported alcohol abusers (Roth and Bean 1985). Those with alcohol problems were more likely than the total sample to be men (94 percent versus 78 percent), were older (median age 41 years versus 33 years), were more likely to be divorced (45 percent versus 20 percent), were less likely to be currently married (3 percent versus 11 percent), and were more likely to have been in jail (87 percent versus 51 percent). The group with alcohol problems had been homeless twice as long; 24 percent of the alcohol abusers had been homeless for 2 years or more, compared with 13 percent of the others in the study.

Homeless persons who drink heavily are especially susceptible to certain health problems (Wright 1985). Trauma is much more prevalent among drinkers than among nondrinkers in the homeless population; a New York study indicated that 42 percent of drinkers showed evidence of trauma, compared with 18 percent of nondrinkers. Homeless problem drinkers run higher risks of thermoregulatory disorders, the most serious of which is frostbite that may lead to gangrenous infection. Peripheral vascular disorders, such as edema and cellulitis, are common. Physical debilitation and poor personal hygiene can lead to ulcers, septicemia, and gangrene. Homeless drinkers are considered to be more susceptible to infestations of scabies and lice. One commonly used treatment for such infestations has been associated with neurological side effects and may be contraindicated for alcohol users. Homeless persons generally exhibit active tuberculosis rates 100 to 200 times the rate observed for the general population. Heavy drinkers are considered to be at greater risk for tuberculosis because of their generally more debilitated condition, and sharing of bottles is a possible source of tuberculosis infection.



## Minority Groups

### Blacks

Blacks are the largest ethnic minority in the United States, numbering more than 27 million in 1983—about 12 percent of the total population and 92 percent of the nonwhite population. Thus, when research studies designate racial groups only as white or nonwhite, data on nonwhites can be considered as reasonably representative of blacks. Despite the large size of the black population and the high rate of alcohol-related problems within this population, relatively little alcohol-related research has focused specifically on blacks (Lex 1985; Herd in press).

Results of national surveys in 1979 and 1983 indicated that blacks of both sexes had higher rates of abstention than whites (Clark and Midanik 1982; Malin et al. 1986). Among drinkers, white men were more likely to be heavy drinkers than black men. The reverse was true for female drinkers, with black women more likely to drink heavily than white women. A large-scale survey in California confirmed these patterns and found significant age-group differences between black and white men (Caetano 1984). Consumption among white men was high among 18- to 29-year-olds but declined after age 30, whereas consumption among blacks was relatively low between the ages of 18 and 29 but rose sharply among those in their 30s.

A national survey in 1984 further confirmed these age-group patterns among black and white men (Herd in press). Among women, the 1984 survey found similar racial differences in the age distribution of drinking patterns. This survey also confirmed higher rates of abstention among blacks for men (29 percent versus 23 percent for whites) and women (46 percent versus 34 percent). However, contrary to earlier findings, white women in the two heaviest drinking categories (those who drink at least once a week and, at least sometimes, consume five drinks at a time) proportionately outnumbered black women, with 13 percent heavy drinkers versus 8 percent for black women (Herd in press).

Among white men, increasing income levels were found to be associated with increases in heavy drinking, but among black men, rates of heavy drinking fell with increasing income. For both black women and white women, increasing income was associated with increases in frequent, as opposed to heavy, drinking.

A nationwide survey of 5,000 high school students in the 10th through 12th grades revealed that there were twice as many abstainers reported among black students as among white students (Lowman et al. 1983). Among black students, 41 percent of females and 34 percent of males reported that they abstained, whereas only 18 percent of white females and 20 percent of white males were self-reported abstainers. Black students who did drink consumed less alcohol and drank less frequently than white students. There were four times as many heavier drinkers among white students, with 16 percent drinking at least once a week and consuming at least five drinks on each occasion. Only 4 percent of blacks drank at that level. Demographic differences did not adequately explain the

large differences in alcohol use, but many of the black abstainers reported that they used marijuana. Although similar levels of marijuana use were reported by both black and white students, 24 percent of black marijuana users were self-reported alcohol abstainers, compared with only 4 percent of white marijuana users.

Blacks, especially black men, are at high risk for certain alcohol-related causes of mortality and morbidity, particularly liver cirrhosis and such associated disorders as fatty liver and hepatitis. Blacks have an extremely high incidence of cancer of the esophagus, with incidence rates several times higher than those for whites (Herd in press). Alcohol is considered to be a major causal factor in the development of this type of cancer (Page and Asire 1985; Cann 1986; Lieber et al. 1986).

The cirrhosis mortality rate was higher for whites than for nonwhites from the mid-1930s until the mid-1950s, when cirrhosis mortality in nonwhites began a steep rise. The nonwhite cirrhosis mortality rate doubled in the 1960s and, between 1950 and 1972, it increased 242 percent, from 7.4 to 25.3 deaths per 100,000 population (NIAAA 1985b). Cirrhosis death rates for whites rose only 58 percent during the same period. Despite a downward trend after 1972, the cirrhosis death rate for nonwhites has continued to far exceed the rate for whites.

Cirrhosis death rates for both white and nonwhite men have been consistently higher than those for women, often more than double the female rate (see figure 6). In 1972, the cirrhosis death rate for nonwhite men was nearly twice the rate for white men, twice the rate for nonwhite women, and more than four times the rate for white women. The rate for nonwhite women increased 203 percent from 1950 to a peak in 1973, compared with an

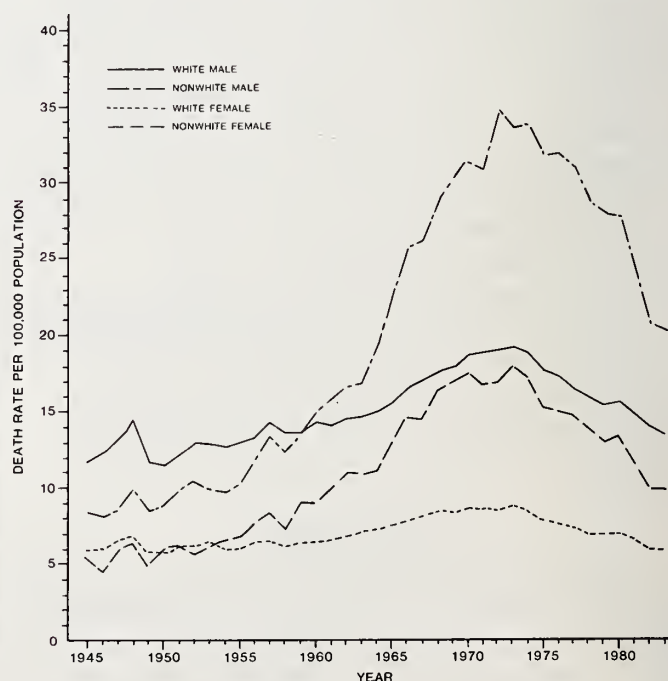


FIGURE 6. Age-adjusted mortality rates from cirrhosis of the liver, by race and sex, United States, 1945-1983.

SOURCES: NIAAA 1985b, 1986a.



increase of 50 percent for white women over the same period. After 1973, there was a steady decline in cirrhosis death rates for all race and sex groups, but the white-nonwhite mortality ratios were unchanged in 1980; nonwhite mortality rates remained nearly twice the white rates (20.0 and 11.1 deaths per 100,000, respectively). The elevated nonwhite mortality rates may reflect the different age patterns of heavy drinking in the black and white populations.

Herd (1985) noted an association between cirrhosis mortality and major demographic shifts in the black population, whereby regional trends in mortality appeared to reflect blacks' migration and urbanization. In major areas of black migration influx, such as the urban North and the coastal South, cirrhosis death rates for nonwhites rose steeply between 1949 and 1970, but rates remained low in the Deep South where there is a large and relatively stable rural black population. In contrast, cirrhosis mortality rates for whites rose more in the Deep South than they did in the urban North during the same period.

A similar geographic pattern emerged in national surveys of clients in alcohol treatment programs. In the urban northeastern States, the proportions of blacks in treatment in 1980 and 1982 were two to three times higher than their proportions in the States' populations. However, in the interior South, the number of blacks in treatment was generally proportional to their representation in the population (Herd 1985).

Despite late onset of heavy drinking, blacks were shown to enter treatment at younger ages than whites. Blacks between the ages of 35 and 44 had the highest rates of admission to treatment programs, whereas the peak ages for whites entering treatment were between 45 and 54 (Herd 1985).

### *Hispanics*

In 1980 there were nearly 15 million Hispanics in the United States, more than 6 percent of the total population (U.S. Bureau of the Census 1980). Hispanics are a heterogeneous group with diverse cultural, national, and racial backgrounds. Hispanic men have relatively high rates of alcohol use and abuse, while Hispanic women have high rates of abstinence.

Alcocer (1982) reviewed the relatively few existing studies of alcohol use by Hispanics in this country. However, these studies did not provide a full epidemiologic picture of alcohol use and abuse by Hispanics because they focused mainly on relatively small and homogeneous populations.

The first large-scale nationwide survey of drinking patterns and alcohol problems in a truly representative sample of Hispanics was conducted by Caetano (in press). The survey found that, among Hispanic women, nearly half (47 percent) abstained and an additional 24 percent drank less than once a month. In contrast, only 22 percent of the men were abstainers, and 36 percent drank heavily or moderately heavily, that is, drank at least once a week and at least sometimes consumed five or more drinks at a sitting. This study also revealed that Hispanic men drink more heavily

in their 30s than in their 20s, with consumption declining only after age 40.

In Hispanics of both sexes, after age 60 there was a significant increase in the number of abstainers as well as a decrease in the number of heavy drinkers. Among women, consumption increased markedly in middle age, with a considerable rise in consumption by women in their 40s and 50s. However, after the age of 60, 88 percent of women abstained or drank less than once a month, and none drank heavily. In both sexes, drinking levels increased with increasing education and income level, a finding that confirmed earlier studies. Persons in the higher income brackets and with higher educational attainment had lower rates of abstention and higher rates of heavy drinking.

Analysis of survey data by national origin showed that Mexican American men had both the highest rate of abstention and the highest rate of heavy drinking when compared with Hispanics of Cuban, Puerto Rican, or other Latin American origin. Mexican American women drank more heavily than women in the other groups but also had a high rate of abstention. Puerto Rican women were predominantly moderate drinkers; they had the lowest rate of abstention and included very few heavy drinkers.

A survey of Mexican Americans in five western States (Christian et al. 1985) also found a relatively high rate of abstention, particularly among women, with 64 percent of women and 25 percent of men abstaining. This study of Mexican Americans also confirmed Caetano's (1984) findings of increased abstention rates in middle age, particularly after the age of 55, and of decreased abstention with increasing levels of education and income.

Comparison of drinking levels by birthplace revealed that first-generation Hispanic men, those born in the United States to foreign-born parents, had decreased levels of abstention and increased levels of heavy drinking, compared with foreign-born Hispanic men (Caetano in press). More than half (54 percent) of first-generation Hispanic men drank heavily or moderately heavily, compared with 38 percent of foreign-born Hispanic men. First-generation Hispanic women had lower rates of abstention but higher rates of infrequent light drinking than women born abroad. Among Hispanic men born abroad, Mexicans had a rate of heavy drinking six times higher than that of any other national group, together with a low rate of abstention. In contrast, foreign-born Mexican American women had a high rate of abstention and almost no heavy drinking.

Self-reported prevalence of drinking-related problems (symptoms of dependence, social problems, health problems, and accidents) was very high among foreign-born Mexican American men. Only 75 percent of foreign-born Mexican American men reported no alcohol problems, compared with 95 percent of foreign-born Puerto Ricans, 98 percent of Cubans, and 81 percent of other Latin American men (Caetano in press).

In contrast to problem rates for white men in the same sample and for men in the general population, the rate of alcohol problems among Hispanic American men did not



drop between their 20s and their 30s but remained high until their 40s. Problem rates among women in their 20s were high. These women reported rates for some problems (salience of drinking behavior, impaired control over alcohol consumption, belligerence, and health problems) not substantially below those of men in the same age group, even though the rate of heavy drinking among the men was eight times higher (Caetano 1984).

### *American Indians and Alaskan Natives*

There are about 1.5 million American Indians and Alaskan Natives in the United States, less than 1 percent of the total population (U.S. Bureau of the Census 1980). American Indians have rates of alcohol abuse and alcoholism several times higher than rates in the general population. However, as pointed out in comprehensive reviews of recent research (Lex 1985; Heath in press), drinking practices and consequent problem levels vary widely across tribal groups. Of more than 280 diverse American Indian populations, some are characterized by binge drinking followed by periods of sobriety, while other groups remain almost totally abstinent. In still other populations, moderate drinking is the norm. Alcohol problems among American Indians appear to have a strong correlation with economic factors such as unemployment and low income levels and with marital and family instability.

American Indian men between the ages of 25 and 44 have the highest rates of alcohol consumption; both total consumption and numbers of drinkers decline after age 40 (Lex 1985). Long-term heavy drinkers over age 40 make up a relatively small proportion of the American Indian population. American Indian adolescents have high rates of consumption, with 42 percent of male drinkers and 31 percent of female drinkers reporting alcohol problems, compared with 34 percent of white male and 25 percent of white female adolescent drinkers (Lex 1985).

The rate of American Indian hospital discharges involving alcohol-related illnesses or injuries in 1979 was more than three times the rate for the general population (Lex 1985). Accidents, liver cirrhosis, alcoholism, homicide, and suicide are among the 10 leading causes of death among American Indians, and all of these are, or may be, alcohol related. Accidents, homicide, and suicide occur most frequently among people in the younger age groups.

Accidents, the second most frequent cause of death among American Indians after heart disease, account for about 20 percent of deaths, and an estimated 75 percent of those accidents are alcohol related (Lex 1985). Accidents account for nearly one-fourth of the deaths among American Indian men and are particularly prevalent among Alaskan Natives. Accidents are consistently the leading cause of death in Alaska, accounting for 23 percent of all deaths in 1983, compared with 4.5 percent for the United States as a whole. The 1983 death rate for accidents was 146 per 100,000 among Alaskan Natives, compared with 82 per 100,000 for all Alaskans and 39 per 100,000 for the general U.S. population (Kelso and DuBay in press).

For the 3-year period from 1977 to 1979, the age-adjusted American Indian and Alaskan Native combined mortality

rate for alcohol psychosis, alcoholism, and alcoholic cirrhosis of the liver was 57.3 per 100,000 population, compared with a rate of 7.4 per 100,000 for the overall population of the United States (Lex 1985). From 1978 to 1983, the alcoholism death rate for Alaskan Natives remained fairly constant at 30 to 36 per 100,000, compared with 7 to 8 per 100,000 for white Alaskans (Kelso and DuBay in press). From 1974 to 1983, Alaskan Natives accounted for more than half of the deaths from alcoholism in Alaska, although they constituted only about 15 percent of the population of the State.

Liver cirrhosis is the fourth-ranked cause of death among American Indians, causing 6 percent of all deaths, compared with 1.4 percent of deaths in the total U.S. population. Using 1980 national mortality statistics, Bertolucci et al. (1985b) estimated that, in 1980, American Indian men lost an estimated 527 years of potential life per 100,000 population due to alcoholic cirrhosis. In comparison, black men lost an estimated 253 years of potential life per 100,000 population, and white men 99 years. The comparable rates for women were 349 years for American Indians, 121 years for blacks, and 40 years for whites.

Homicide is the cause of 3.3 percent of deaths among American Indians, more than double the rate for the U.S. population as a whole. An estimated 90 percent of Indian homicide deaths are alcohol related (Lex 1985).

The rate of suicide among American Indians, about 22 per 100,000 population, is almost double the rate for the overall population (Heath in press). However, among tribes, rates vary from 8 to 120 per 100,000 population. Suicide rates are particularly high among Alaskan Natives, with a high in 1973 of 518 suicide attempts per 100,000 population (Kelso and DuBay in press). Between 1975 and 1981, the suicide rate among Alaskan Natives declined, dropping from 43 percent to 18 percent of all Alaskan suicides. An estimated 80 percent of all American Indian suicide deaths are alcohol related (Lex 1985).

American Indian women appear to be particularly susceptible to alcohol-related problems. Although they drink less than men, they account for nearly half of all American Indian cirrhosis deaths. Also, American Indians appear to be at particular risk for FAS. This is discussed in detail in chapter V.

### *Asian Americans and Native Hawaiians*

Asian Americans, who make up less than 2 percent of the population of the United States, have very low levels of alcohol use and abuse. A comparison of racial patterns of alcohol consumption among whites, blacks, Hispanics, and Asians in Oakland, Calif., found that Asian Americans of both sexes drank significantly less than whites, blacks, or Hispanics (Klatsky et al. 1983).

It is often assumed that all Asian Americans have similar drinking practices and similar problem levels regardless of national origin. However, Asian Americans have a great diversity of cultural backgrounds, with origins in China, Japan, the Philippines, Korea, India, Vietnam, and other Asian countries, and recent studies have shown that there are significant differences in consumption patterns among



Asian Americans of different origins (Klatsky et al. 1983; Kitano et al. 1985; Sue et al. 1985; Ahern in press; Murakami in press).

A survey comparing the drinking patterns of Chinese, Japanese, and Koreans in Los Angeles with those of other Californians showed very high levels of abstention, with 67 percent of Koreans, 55 percent of Chinese, and 47 percent of Japanese abstaining, compared with 13 percent of the general population of California (Kitano et al. 1985; Sue et al. 1985). Abstention rates were significantly higher for Asian females than for males, with 81 versus 56 percent for Koreans, 74 versus 48 percent for Chinese, and 63 versus 36 percent for Japanese.

The Chinese in this study had significantly lower rates of heavier drinking (defined as four or more drinks per day) than the other groups, with only 8 percent drinking at this level, compared with 21 percent of Japanese, 14 percent of Koreans, and 17 percent of other Californians. Among males, the Japanese and Koreans had the highest proportion of heavy drinkers (26 and 24 percent, respectively), while 12 percent of Chinese and 16 percent of other California men were heavier drinkers. Among females, there were no Chinese in the heavier-drinker category and only 0.8 percent of Koreans, compared with 12 percent of Japanese and 18 percent of other California women.

Murakami (in press), in a recent survey of alcohol consumption by the four major ethnic groups in Hawaii, found that Native Hawaiians consumed somewhat less alcohol than Caucasians but significantly more than Japanese or Filipinos. In all groups, men drank more than women. The proportion of heavier drinkers, defined as those who consumed 1 or more ounces of ethanol (two or more drinks) per day, among Native Hawaiians was 11 percent, compared with 14 percent for Caucasians, 7 percent for Filipinos, and 5 percent for Japanese. More than half the Japanese and Filipinos were abstainers, compared with 41 percent of Native Hawaiians and 31 percent of Caucasians.

Ahern (in press), in a review of earlier studies, presented data suggesting that Native Hawaiians, as well as other non-Caucasian ethnic groups, are underrepresented in treatment facilities in proportion to their estimated numbers of heavier drinkers, defined as those who consumed 2 or more ounces of pure alcohol (four or more drinks) per day during the month preceding the survey. In 1979, 41 percent of all such heavy drinkers in Hawaii were Caucasian, but they represented 71 percent of treatment admissions. Native Hawaiians accounted for 19 percent of the State's alcohol abusers in 1979 but only 10 percent of admissions. Japanese, Filipinos, and Chinese had lower proportions of alcohol abusers (11, 9, and 2 percent, respectively), and these groups accounted for even lower percentages of treatment admissions (4, 2, and 0.2 percent, respectively).

Between 1975 and 1980, Native Hawaiians were at less risk than Caucasians for liver cirrhosis, with an estimated 6.8 deaths per 100,000 population versus 12.1 per 100,000 for Caucasians. However, alcoholic Caucasians had significantly lower death rates from liver cirrhosis than Japanese,

Chinese, and Filipinos, and Caucasian male alcoholics had significantly fewer cases of organic brain syndrome. During this period, Native Hawaiians were at greater risk than the general State population for only three of eight alcohol-related causes of death: homicide, motor vehicle accidents, and suicide (Ahern in press).

## COSTS OF ALCOHOL ABUSE

In 1980, alcohol abuse in the United States was estimated to cost \$89.5 billion (see table 12). Lost employment and reduced productivity (\$54.7 billion) accounted for more than half this amount. Health care for accidents and illnesses related to alcohol abuse, including alcoholism, liver cirrhosis, cancer, and diseases of the pancreas, was estimated to cost \$10.5 billion. (These estimates are not comparable to an earlier assessment of costs based on 1977 data because of differences in methodology, among other factors.)

Projections of the 1980 estimate to future years, adjusting only for inflation and population changes, indicate that, in 1983, alcohol abuse cost the United States almost \$117 billion (see table 13). Of this amount, nearly \$71 billion is attributed to lost employment and reduced productivity and \$15 billion to health care costs.

## SUMMARY

In 1984, the estimated per capita consumption of alcohol in the United States was the equivalent of 2.65 gallons of pure alcohol. This is the amount of alcohol one would obtain from approximately 50 gallons of beer, or 20 gallons of wine, or more than 4 gallons of distilled spirits. This was the lowest level of consumption since 1977. After reaching a peak in 1980 and 1981, apparent consumption began a gradual decline. In the single year from 1983 to 1984, apparent per capita consumption decreased or remained unchanged in 43 States and the District of Columbia; only 7 States showed an increase.

Half the alcohol consumed in the United States is accounted for by the 10 percent of the drinking population who drink the most heavily. About one-third of the U.S. population are light drinkers, one-third are moderate-to-heavy drinkers, and one-third are abstainers. There are more abstainers among women than among men, and among older people of both sexes than among younger adults.

Alcohol is associated with a wide variety of diseases and disorders. The greatest chronic health hazard of alcohol is liver disease. In 1983, cirrhosis of the liver caused 28,000 deaths and was the ninth leading cause of death at all ages in the United States. Cirrhosis death rates are higher for men than for women and higher for nonwhites than for whites. Cirrhosis mortality has been declining, and the mortality rate for 1983 was the lowest recorded since 1959.

Accidental death, suicide, and homicide are significant causes of death, particularly for young men under age 34. Nearly half of these violent deaths are alcohol related, and victims are intoxicated in about one-third of drownings,

TABLE 12. *Costs to society of alcohol abuse, drug abuse, and mental illness, United States, 1980*

Types of costs	Costs (\$ millions)			Total <sup>e</sup>
	Alcohol abuse	Drug abuse	Mental illness	
Core costs				
Direct				
Treatment	9,487	1,200	20,961	31,647
Support	984	243	2,597	3,823
Indirect				
Mortality <sup>a</sup>	14,456	1,980	7,196	23,632
Morbidity <sup>b</sup>	54,680	26,028	21,664	102,372
Reduced productivity <sup>c</sup>	(50,575)	(25,716)	(3,122)	(79,413)
Lost employment	(4,105)	(312)	(18,542)	(22,959)
Total <sup>e</sup>	79,607	29,451	52,418	161,476
Other related costs				
Direct				
Motor vehicle crashes (property loss)	2,185	<sup>d</sup>	—	2,185
Crime <sup>b</sup>	2,347	5,910	870	9,127
Public	(2,062)	(4,454)	(635)	(7,151)
Private	(261)	(1,345)	(235)	(1,841)
Property loss/damage	(24)	(111)	(—)	(135)
Social welfare programs	38	2	201	241
Other	2,912	537	659	4,108
Indirect				
Victims of crime	172	845	—	1,017
Crime careers	—	8,725	—	8,725
Incarceration	1,801	1,466	88	3,356
Motor vehicle crashes (time loss)	464	<sup>d</sup>	—	464
Total <sup>e</sup>	9,919	17,485	1,818	29,222
Total <sup>e</sup>	89,526 <sup>c</sup>	46,936 <sup>c</sup>	54,236 <sup>c</sup>	190,698

SOURCE: Adapted from Harwood et al. 1984.

<sup>a</sup>At 6 percent discount rate.<sup>b</sup>Components are indicated in parentheses.<sup>c</sup>Total costs for each of the three disorders are not comparable because the completeness of data available for each category varied significantly. For example, the estimate of reduced productivity is relatively complete for alcohol abuse, partially complete for drug abuse, and incomplete for mental illness.<sup>d</sup>Although costs are hypothesized to occur in this category, data are insufficient for a reliable estimate.<sup>e</sup>Totals may not add exactly because of rounding.

homicides, boating deaths, and aviation deaths, and in about one-fourth of suicides.

There was a significant decrease in the number of alcohol-related traffic fatalities from 1980 to 1984. The proportion of fatally injured drivers who were legally intoxicated (in most States, having a blood alcohol concentration of 0.10 percent or more) dropped from 50 percent in 1980 to 43 percent in 1984.

An estimated 18 million persons 18 years old and older experience problems as a result of alcohol use. These may be dependence symptoms, such as binge drinking or loss of control over drinking behavior, or negative personal consequences, such as problems with health, work, or personal relationships. Patterns in problem prevalence tend to parallel patterns of heavy drinking with regard to sex, age, and ethnic background.

Nearly half of convicted jail inmates were under the influence of alcohol at the time of committing the criminal offense, and more than half of those who had been drinking were drunk at the time. More than half of the persons convicted of violent crimes had been drinking at the time of the offense.

Women drink significantly less heavily than men and have fewer drinking-related problems, but the level of drinking for women in their middle years (ages 35 to 64) has increased. Higher rates of gynecologic and obstetric problems, including stillbirth and birth defects, are associated with higher drinking levels.

Drug use (especially marijuana use) among high school seniors declined from 1980 to 1984 and leveled off in 1985, except for cocaine use, which increased. However, alcohol use continued a steady decline from 1980 to 1985. In 1985, 1 out of 20 high school seniors drank every day, 92 percent had used alcohol at least once, and 30 percent reported that most or all of their friends got drunk at least once a week. One-third of adolescents aged 16 to 18 reported that most or all of their friends drank regularly.

People over the age of 65 consume less alcohol than younger adults, and they have a lower prevalence of alcohol abuse. Decreases in individual consumption may be due to the lowered tolerance for alcohol that is associated with aging. Elderly long-term alcohol abusers are at high risk for adverse health effects. Major late-life stresses may affect levels of alcohol abuse in the elderly.



TABLE 13. *Economic costs to society of alcohol abuse and alcoholism, United States, 1983*

Types of costs	Costs (\$ millions)
Core costs	
Direct	
Treatment <sup>a</sup>	\$13,457
Health support services	1,549
Indirect	
Mortality <sup>b</sup>	18,151
Reduced productivity	65,582
Lost employment	5,323
Other related costs	
Direct	
Motor vehicle crashes	2,697
Crime	2,631
Social welfare administration	49
Other	3,673
Indirect	
Victims of crime	194
Incarceration	2,979
Motor vehicle crashes	590
Total	\$116,875

SOURCE: Harwood et al. 1985.

<sup>a</sup>For alcohol abuse and alcoholism, liver cirrhosis, other illnesses, motor vehicle crashes, and other injuries.

<sup>b</sup>At 6 percent discount rate.

There are an estimated 250,000 to 350,000 homeless persons in the United States, including growing numbers of women, children, the elderly, the unemployed, minorities, and the mentally ill. The homeless have a high rate of alcohol-related problems and are particularly susceptible to many health problems.

Blacks have higher rates of abstention than whites. Among drinkers, black men are less likely to drink heavily than white men, but the reverse is true for women. The incidence of alcohol-related medical problems, particularly liver cirrhosis and cancer of the esophagus, is very high among blacks. Cirrhosis mortality rates for blacks are twice as high as the rates for whites.

Hispanic men in this country have a high rate of alcohol use and abuse and a high rate of cirrhosis mortality. Nearly half of the Hispanic women are abstainers, and another fourth drink less than once a month, while less than one-fourth of the men abstain. First-generation American-born Hispanic men drink more heavily than foreign-born Hispanics.

American Indians and Alaskan Natives appear to have very high rates of alcohol abuse and alcoholism, although there is great variation among tribal groups. Even though many tribes remain almost totally abstinent, the rate of alcohol-related illness and injury among American Indians is three times the rate for the general population. Accidents, most of them alcohol related, are the second most common cause of death and account for nearly one-fourth of deaths among American Indian men. Homicide and suicide rates are double the rates for the general population. Liver cirrhosis is the fourth-ranked cause of death among American Indians.

Asian Americans, regardless of national origin, have very low levels of alcohol use and abuse. The percentage

of abstainers is very high in all Asian American groups, particularly among women, with the highest abstention rates among Koreans and Chinese. Chinese of both sexes and Korean women have the lowest levels of heavier drinking, and those with the highest levels among males are Japanese and Koreans. In Hawaii, Native Hawaiians have higher rates of consumption than Japanese, Filipinos, or Caucasians.

Complex interactions of demographic, social, economic, and biological factors determine whether a person drinks, how much and how often that person drinks, and what the individual response will be to alcohol. Age, sex, and ethnic background are particularly significant determinants of a person's drinking patterns and susceptibility to drinking problems. Successful prevention and treatment of alcohol abuse and alcoholism must be based on a knowledge and understanding of these factors.

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# Genetics and Alcoholism

**A**mong the most compelling studies indicating a genetic contribution in at least some types of alcoholism have been those that compared the incidence and patterns of alcoholism in children who were adopted from their biological parents at an early age. The studies, which were described in the *Fifth Special Report to the U.S. Congress on Alcohol and Health* (USDHHS 1984), indicated that children of alcoholics raised by nonalcoholic foster parents had a much higher prevalence of alcoholism than did the adopted children of nonalcoholic biological parents.

Further evidence for the operation of genetic factors in alcoholism has come from selective breeding experiments. Thus animal lines have been produced that differ in susceptibility to various effects of alcohol on the central nervous system (Kakihana et al. 1966; McClearn and Kakihana 1973; Riley et al. 1977; Crabbe et al. 1981, 1983), including different susceptibility to alcohol tolerance and severity of withdrawal symptoms (Grieve et al. 1979; Tabakoff et al. 1980; Crabbe et al. 1981). Lines have also been bred that differ in their rates of alcohol metabolism (Thurman 1980). Finally, selective breeding has yielded alcohol-preferring and alcohol-nonpreferring lines (Eriksson 1968; Li et al. 1979). The ability to produce such animal lines is excellent evidence that susceptibility to important effects of alcohol can be inherited.

These demonstrations that genetic factors can be involved in the development of alcoholism and in responses to alcohol are significant achievements, but they immediately raise more fundamental questions: Exactly what is inherited? Which genes are involved in the transmission of this susceptibility? Through what mechanisms do the products of those genes act to make some people crave alcohol? Can such people who have inherited the susceptibility to alcoholism be identified by specific biochemical or physiological tests, so they can be counseled about their susceptibility before they even start drinking?

These are important questions, centered on the fundamental mechanisms that give rise to alcoholism. The search for the answers is one of the most exciting areas in the field of alcohol research, because the ultimate benefits of understanding these mechanisms may well be greatly improved methods for preventing and treating this disease.

This chapter presents selected research findings in this area that have been published since the *Fifth Special Report*. Earlier reports are also cited when necessary to put more recent research in proper context and show its antecedents. The chapter begins with a review of adoption studies done in Scandinavia that provide strong evidence that genetics plays an important role in human susceptibility to alcoholism. The remainder of the chapter deals with the search for specific genetic differences between persons who are at risk of alcoholism and those who are not: neurophysiological differences, neuropsychological differences, and biochemical differences.



## SCANDINAVIAN ADOPTION STUDIES

The observation that alcoholism tends to run in families is a very old one but, until recently, lack of appropriate studies has made it impossible to know whether this familial clustering is due to heredity, environment, or perhaps both. Recent research has provided evidence that both heredity and environment are involved in the genesis of many cases of alcoholism.

Several studies have shown that the sons of alcoholics are many times more likely to become alcoholic than are the sons of nonalcoholics (Goodwin 1971; Goodwin et al. 1973, 1974; Cadoret and Gath 1978; Cotton 1979). These earlier studies suggested that genetic transmission of one or more biological characteristics may predispose the sons of alcoholics to alcoholism. An inherited predisposition to alcoholism has also been found in women and is evidently transmitted through the mother. Bohman et al. (1981) found a threefold excess of alcohol abusers among women who were born to alcoholic mothers but were adopted during the first few months of life by nonrelatives.

A study in Denmark by Goodwin et al. (1973) of 5,483 persons who had been adopted at an early age revealed that the sons of alcoholics who had been adopted by other families were more than three times as likely to become alcoholic as the adopted sons of nonalcoholics. A few years later these findings were confirmed in a study of 2,324 adoptees in Sweden by Bohman (1978). In the Swedish study, male adoptees whose biological fathers were severely alcoholic had a 20 percent incidence of alcohol abuse, compared with 6 percent in the adopted sons of nonalcoholics. Male adoptees whose biological mothers were alcohol abusers had a 33 percent incidence of alcohol abuse compared with 19 percent in the control group, although the difference in this case was not statistically significant.

These adoption studies strongly supported the hypothesis that genetics contributes to susceptibility to alcoholism. The alcoholic adoptees had been separated from their biological parents, and thus from any predisposing environmental influences arising from an alcoholic home, before the age of 3 and in most cases during the first few months of life. The predominant environmental influence therefore came from their adoptive homes, not from the stressful home life that might be associated with parental alcoholism. Nevertheless, in both studies sons adopted from alcoholics had about a threefold greater chance of becoming alcohol abusers or alcoholics.

### The Relative Contributions of Heredity and Environment

More recent studies of Swedish adoptees (Bohman et al. 1981, 1984; Cloninger et al. 1981; Cloninger 1983) have examined the interaction of heredity and environment and have sought to determine what characteristics of biological and adoptive parents influence the risk of alcohol abuse in the adoptees. They have also investigated the question of whether the genetic predisposition to alcoholism can be expressed in other psychopathological ways, depending on the environment and sex of the individual. The investiga-

tors selected 862 men and 913 women of known paternity who had been adopted before the age of 3 by nonrelatives. Of these 1,775 subjects, 627 (35.3 percent) had a biological parent who abused alcohol. The subjects were grouped according to both congenital background and adoptive home environment, and each group was analyzed to determine how adoptees with particular kinds of congenital background react to different types of adoptive placement. Degree of alcoholism (none, mild, moderate, or severe) was assessed in all the subjects, and correlations were sought between these ratings and a variety of factors—including biological factors in the biological parents and environmental factors in the adoptive parents.

This was not a clinical study. Data on alcohol use, characteristics of biological and adoptive parents, and other relevant factors were not obtained from the subjects themselves but from official sources such as adoption agencies; insurers; hospitals; police; social welfare organizations; and the Swedish Temperance Board, which investigates reports of alcohol abuse and alcoholism and maintains detailed records. It has been found, however, that alcoholics identified through official registries in this cohort of adoptees are a representative sample of all alcoholics and that their placement in adoptive homes was random (Ojesjö and Hagnell 1980).

Two categories of alcoholic families were identified in these studies—those in which alcoholism developed only in men and those in which it developed in both men and women. Alcoholism was significantly more prevalent in the adopted sons of alcoholic biological fathers: 22.8 percent of the sons of alcoholic biological fathers were alcoholic, compared with 14.7 percent of the sons who did not have an alcoholic biological parent. Alcoholism in the biological mother also was a predisposing factor: 28.1 percent of the sons of alcoholic biological mothers were alcohol abusers, compared with 14.7 percent of sons who did not have an alcoholic biological parent.

An effect of parental alcoholism was also found in adopted women. Daughters adopted from alcoholic mothers had more than three times the frequency of alcohol abuse than the daughters adopted from nonalcoholic parents: 10.8 percent of the daughters of alcoholic biological mothers were alcohol abusers, compared with 2.8 percent of daughters who did not have an alcoholic biological parent.

The evidence from these studies is compelling: biological inheritance can be a major factor in the development of alcohol abuse and alcoholism. Furthermore, these studies have revealed the existence of two forms of inherited predisposition—one that is strongly influenced by postnatal environment, and one in which the development of alcoholism is strongly influenced by the sex of the individual.

### Two Forms of Inherited Alcoholism

Analysis of the data in the recent Swedish adoption studies have revealed the existence of two types of genetic predisposition to alcoholism (Bohman et al. 1981, 1984; Cloninger et al. 1981; Cloninger 1983). The more common type, called milieu-limited (or Type I) alcoholism, accounts



for most cases of alcoholism. It occurs in both men and women, is usually not severe, and is associated with mild, untreated, adult-onset alcohol abuse in either biological parent. The biological parent with milieu-limited alcoholism also tended to have no significant record of "criminality" (a term very broadly defined in these studies to include any kind of legal misconduct—whether infractions, misdemeanors, or felonies—that brought the biological parent to the attention of law enforcement authorities). It is called milieu-limited alcoholism because its occurrence and severity in an adoptee was influenced by the postnatal environment. Thus, its manifestation required both a genetic predisposition and environmental provocation. Data analysis showed that if only one of these factors was present in a male or female adoptee, the risk of alcohol abuse was about the same as in the general population. If both factors were present, the risk was doubled and the severity of alcohol abuse was determined by the degree of postnatal provocation.

The other type of hereditary predisposition found in the Swedish studies is called male-limited (or Type II) alcoholism. This severe type of predisposition is found only in men, accounting for about 25 percent of all male alcoholics in the general population, and its transmission appears to be unaffected by the environment. In families with male-limited susceptibility, alcohol abuse was nine times more frequent in the adopted sons regardless of their postnatal environment. Male-limited susceptibility was associated with severe alcoholism in the biological father but not with alcohol abuse in the biological mother. The biological father also tended to have a record of more serious criminality (as defined in these studies—see preceding paragraph). Male-limited alcoholism frequently developed in the biological fathers when they were adolescents and was associated with episodes of extensive treatment. Although postnatal environment apparently cannot prevent the development of male-limited alcoholism in those predisposed to it, unless they abstain, postnatal environment may influence the severity of the disease. Adoptees with this form of alcoholism generally were less severely alcoholic than their fathers, possibly reflecting a better life in their adoptive homes.

No evidence was found that men with male-limited alcoholism can transmit the same susceptibility to their daughters. However, the Swedish adoption studies did find that adopted women whose biological fathers had this form of hereditary alcoholism had a greater frequency of diversiform somatization—a psychosomatic condition characterized by frequent complaints of pain or discomfort, usually medically unexplained, in various parts of the body. This suggests that women may inherit the same genetic factors that lead to male-limited alcoholism but express those factors in different ways.

An important finding in these adoption studies is that environmental provocation for the expression of milieu-limited predisposition did not include alcoholism in the adoptive parents. No association at all was found between alcoholism in adoptive parents and alcoholism in adoptees. The only significant risk factor in the adoptive parents was

low socioeconomic status of the adoptive father. Adoptees with milieu-limited susceptibility were not at increased risk for alcoholism unless two factors were present: an adoptive father who had low socioeconomic status and a biological parent who abused alcohol.

How low socioeconomic status in an adoptive father could provoke expression of milieu-limited alcoholic predisposition in an adopted son or daughter is a complex issue. In general, it seems likely that a number of family life factors that accompany low socioeconomic status could impinge on a nervous system and a personality already made vulnerable by genetic factors, with one result being excessive drinking leading to alcoholism. Possible points of vulnerability were explored in a recent theoretical article by Cloninger et al. (in press). This paper examined the relationship of certain personality traits, postulated to be based on inherited neurochemical differences, with forms of inherited susceptibility to alcoholism. On the basis of several lines of evidence, characteristic personality traits were linked to both male-limited and milieu-limited alcoholism. In the Swedish adoption studies, men with male-limited alcoholism (or women with diversiform somatization) were high in a trait called novelty-seeking, which is characterized by impulsiveness, quick temper, excitability, and a tendency to be unusually sensitive to pain. Milieu-limited alcoholics were high in reward dependence—a tendency to be ambitious, sentimental, and moody and to depend greatly on rewards such as social attachments, wealth, power, and food, as well as substances of abuse such as alcohol. Thus, it may be that milieu-limited alcoholics have a certain kind of inherited neurochemical constitution that is manifested as a personality highly dependent on rewards. If so, it is conceivable that a person so constituted might first become psychologically dependent on alcohol for its rewarding properties and finally, after repeated exposure, become chemically dependent on it, i.e., addicted.

Regarding low socioeconomic status of the father as a risk factor for expression of milieu-limited susceptibility, the family dynamics involved are undoubtedly very complex, and much research will be needed to understand fully how they can push the susceptible individual toward alcohol abuse and alcoholism. However, recent research (Sigvardsson et al. 1986) indicates that low socioeconomic status is strongly associated with an attitude that becoming intoxicated is recreation—fun. These investigators report that drinking to become intoxicated, indeed an attitude that this is synonymous with having a good time, is frequent among members of lower socioeconomic groups. This could be an important reason why low socioeconomic status was found to be the major environmental provocation for milieu-limited alcoholism in the Swedish adoption studies. It is not difficult to imagine how individuals with milieu-limited susceptibility growing up in such an environment could readily incorporate frequent "drinking to get drunk" as part of their repertoire of reward-seeking activities.

In any case, it is clear from adoption studies, as well as from other kinds of studies, that a significant risk factor for



the development of alcoholism is to have first-degree relatives who are alcoholic, especially to be the son of a male alcoholic. Practically all the studies designed to identify specific genetic markers of susceptibility—the subject of the rest of this chapter—have used the same definition of being at risk for alcoholism: having alcoholism in the family.

It would be erroneous to conclude, however, that every alcoholic or alcohol abuser harbors a genetic predisposition to alcoholism. Numerous alcoholics do not have alcoholic first-degree relatives, and it is still valid to think that many cases of alcoholism arise from psychological, social, and cultural causes, not genetic ones. Nor is a fatalistic attitude about alcoholism warranted by these studies. Sporadic, nonfamilial alcoholism is preventable and treatable. So is milieu-limited alcoholism. And although male-limited alcoholism may be difficult to treat, its effects can at least be mitigated.

Alcoholics who have a family history of alcoholism, and therefore a possible genetic basis for their disease, should not despair but should keep in mind that other diseases also have a genetic component. It is known, for example, that genetics plays a major role in diabetes. Yet diabetics can be helped, especially when they take responsibility for their own recovery. The same is true of alcoholics.

In summary, both men and women can have milieu-limited alcoholism, and either sex can genetically transmit the susceptibility to either a son or a daughter. Only men can have or transmit male-limited alcoholism, a much more severe form of alcoholism that is difficult to treat, typically begins early in life, and in the Swedish studies was found associated with criminality in the biological father.

These two types of inherited predisposition are referred to again later in this chapter, in the Biochemical Differences section, in the discussion of a recent study that confirmed the milieu-limited (Type I) and the male-limited (Type II) typology in a clinical population of diagnosed alcoholics. This recent study revealed a significant biochemical difference—namely, activity of the enzyme monoamine oxidase—in these two types of alcoholics.

## NEUROPHYSIOLOGICAL DIFFERENCES

### Electrophysiological Studies: Electroencephalograms in the Children of Alcoholic Fathers

Among the distinctive biological variables in alcoholics that have been examined (see reviews by Mendelson and Mello 1979 and by Begleiter and Platz 1972) are certain electroencephalographic (EEG) patterns. A number of earlier investigations found that resting-state EEG recordings in awake alcoholics, taken when the subjects were not under the influence of alcohol, tend to contain excess high-frequency waves (fast EEG activity) and are deficient in alpha, theta, and delta activity (Davis et al. 1941; Funderburk 1949; Little and McAvoy 1952; Funkhouser et al. 1953; Naitoh 1973; Jones and Holmes 1976). Other studies have shown that the pattern of fast EEG activity is genetically transmitted (Vogel 1958, 1970; Young et al. 1972; Propping 1977).

These earlier findings led Gabrielli et al. (1982) to propose that fast EEG activity should be found in the male children of alcoholics but not in the female children of alcoholics. The investigators tested the hypothesis in a sample of 265 Danish children of both sexes ages 11 to 13. The test group consisted of children of schizophrenic, psychopathic, or character disordered parents and included 27 children of alcoholics, whereas the control group consisted of the children of normal parents.

As predicted by the hypothesis, the sons of alcoholics (but not the daughters) showed a significant excess of fast EEG activity in comparison with controls. This finding led the investigators to propose that fast EEG activity could be a potential marker of genetic predisposition to alcoholism. A possibility that the fast EEG pattern might be due to inherited biological factors associated with psychiatric diagnosis, rather than to alcoholism, in the parents was considered unlikely by these authors because other studies (reviewed by Mednick and Volavka 1980) have shown that psychopathy is associated with slow EEG activity.

Other studies have measured the effects of administered alcohol on the EEG of men considered at risk for alcoholism. Pollock et al. (1983) examined alpha wave activity in a group of men ages 19 to 21 to test the hypothesis that subjects at high risk for alcoholism will show greater alpha wave changes after alcohol administration than control subjects will. A group of 44 high-risk sons of alcoholics was compared with a control group of 28 sons of nonalcoholics matched with the study group for age and social class. After a low dose of alcohol (0.5 g/kg of 95 percent ethanol), 2-minute EEG recordings were obtained at 30, 60, and 120 minutes, and blood alcohol levels were measured at 40 and 130 minutes.

Although blood alcohol levels failed to distinguish the high-risk from the low-risk subjects, quantitative measurement of EEG alpha activity did reveal differences in the two groups. The high-risk subjects showed greater increases of slow alpha energy and greater decreases of fast alpha energy after alcohol administration than controls. The high-risk subjects also showed greater decreases in alpha frequency after alcohol administration. These findings led the investigators to suggest that subjects at high risk for alcoholism are physiologically more sensitive to alcohol than control subjects.

### Electrophysiological Studies: Studies of Evoked and Event-Related Potentials

Advances in computer technology have enhanced two newer EEG techniques for examining subtle functional deficits in the brain. Evoked potential (EP) techniques measure the brain's electrical response to particular external stimuli. Event-related potential (ERP) techniques measure electrical events in the brain that arise during the processing of information. Features of the EP and ERP recordings, which are obtained from scalp electrodes, reflect aspects of brain function related to integrative processes. By allowing the simultaneous measurement of electrophysiological events and behavior, these techniques can reveal the level of brain functioning and can provide



information on the functional integrity of neuroanatomical systems. Application of these techniques to the study of chronic alcoholics has demonstrated functional brain abnormalities associated with alcoholism (Porjesz and Begleiter 1981, 1983).

Several studies have shown that ERPs are sensitive indicators of different aspects of sensory, cognitive, and language functions in normal persons (Donchin et al. 1978; Starr et al. 1978; Gaillard and Ritter 1983; Hillyard and Kutas 1983). One particular ERP feature, the P3 wave, has received considerable attention and has been found to have reduced amplitude in many alcoholics (Pfefferbaum et al. 1979; Porjesz and Begleiter 1979; Begleiter et al. 1980; Garozzo 1980). These P3 wave deficits in alcoholics were originally presumed to be a consequence of chronic alcohol abuse. New evidence suggests, however, that they may precede the onset of alcohol abuse and alcoholism and may be a marker of genetic susceptibility.

Begleiter et al. (1984), noting evidence that EP waveforms are genetically determined, postulated that P3 wave deficits may be genetically determined antecedents of alcoholism rather than consequences of it. The investigators tested this hypothesis by measuring ERPs in 25 boys age 12 who were at high risk of alcoholism because their fathers were alcoholics. ERP data from this group were compared with those obtained from a control group of 25 boys, matched for socioeconomic status and age, who had no family history of paternal alcoholism. None of the subjects had ever drunk alcohol or used illicit drugs. Significant differences in the P3 voltage were found between the two groups. The high-risk boys showed a pattern of significantly reduced P3 voltage similar to that previously seen by these investigators in abstinent chronic alcoholics (Porjesz and Begleiter 1981, 1983). This similarity, together with a separate finding that abnormal P3 amplitude does not revert to normal in chronic alcoholics even after continued abstinence (Porjesz and Begleiter 1985), supports the hypothesis that decrements in P3 voltage found in chronic alcoholics are present before alcohol abuse even begins.

These findings of anomalous P3 waves in young, non-drinking sons of alcoholics are particularly interesting because they were obtained without administering alcohol to the subjects. The findings have recently been replicated in a study comparing ERPs in high- and low-risk young male social drinkers, none of whom had progressed to problem drinking (O'Connor et al. in press).

In addition to P3 abnormalities in the ERP, abnormal auditory brain stem potentials have been found in alcoholics (Begleiter et al. 1981; Chu 1985). Auditory brain stem potentials (ABPs) are EPs generated in the brain stem in response to audible sounds, typically clicks generated electronically, and they reflect the successive activation of various brain centers and nerve tracts involved in the early processing of auditory signals.

In view of the similarity in P3 findings between abstinent alcoholics and boys at high risk for alcoholism, Begleiter et al. (in press) compared ABPs in 23 boys ages 7 to 13 who were sons of alcoholic fathers with 23 sons of nonalcoholic

fathers who were matched for age, socioeconomic status, and school grade. As in the previous study, none of the subjects had ever used alcohol or illicit drugs. Unlike the findings with the P3 wave, however, no significant difference in ABPs was found between high- and low-risk boys. This result suggests that although P3 deficits may be antecedents of alcoholism in some high-risk individuals, the ABP deficits seen in abstinent alcoholics may be consequences of alcoholism. The reasoning is that if abnormal ABPs in alcoholics were antecedents of alcoholism, they also should be detectable in boys at high risk for alcoholism.

Other studies of P3 differences have used challenge doses of alcohol administered to high- and low-risk adults. For example, an ERP study (Elmasian et al. 1982) compared P3 responses in 30 young men who were moderate drinkers but had a family history of alcoholism with a control group of young men who drank moderately but had no family history of alcoholism. The investigators reported that characteristics of the P3 wave following administration of either a moderate dose of alcohol or a placebo could differentiate between the two groups. The observed alteration was a rapid and prolonged decrease in amplitude of the P3 wave in the high-risk group (figures 1a and 1b).

Because all subjects in the study by Elmasian et al. expected to receive alcohol, a possible interpretation suggested by the investigators is that neurological features in the brains of men with alcoholic fathers are such that even expectancy of alcohol produces characteristic brain waves. Another possibility suggested by the investigators is that higher alcohol consumption in the mothers of the high-risk group during pregnancy, presumably as a corollary of having an alcoholic spouse, might have affected brain development in the high-risk group. Or it could be that putative genetic factors that predispose sons of alcoholic fathers to develop alcohol dependence may also alter certain brain functions and that these alterations are manifested as an altered P3 wave. Neville and Schmidt (1985) examined each of these three possibilities in a second series of studies involving 20 young men, divided equally between those whose fathers were alcoholics and those whose fathers were not. To examine the possible role of an alcohol-related experimental setting on the observed group differences, the 20 subjects were not given alcohol or placebo and were not made aware that the study was alcohol related. To control for possible effects of maternal alcohol consumption during pregnancy, the mothers of all subjects were extensively interviewed to determine their current and past use of alcohol and other drugs.

A variety of ERP measurements made in association with specific tasks performed by the subjects suggested that neither alcohol administration nor alcohol-related expectancies were needed to observe ERP differences between high- and low-risk young men. Nor were group differences affected by differences in maternal alcohol consumption. Thus, it may indeed be that under certain circumstances the ERP reflects a genetically influenced susceptibility to alcoholism.



Reports that subjects judged at high risk for alcoholism tend to perform more poorly on language and memory tests (Hegedus et al. in press; Tarter et al. in press) prompted Schmidt and Neville (1985) to measure ERPs in high-risk (having alcoholic fathers) and low-risk (having nonalcoholic fathers) young men while they performed a visual language processing task. All the subjects were social drinkers. Major differences were found between the groups in an ERP component called the N430 wave. The amplitude of the N430 was significantly smaller in the men with a family history of alcoholism, and its latency in these subjects (i.e., the time it took to appear) was linearly related to the amount of alcohol they drank per occasion, though not to the frequency of such occasions. These

findings suggest that certain brain functions associated with this language-processing task are different in men at high and low risk for alcoholism and that social drinking may have more pronounced effects on language-relevant brain functions in men with a family history of alcoholism.

Although these studies clearly show an association between ERP characteristics and the presumed risk of developing alcoholism, the precise physiological meaning of these ERP differences in high- and low-risk persons is unknown. Further research, including studies in animals, is needed to understand fully the meaning of the biochemical and cellular processes that give rise to these electrophysiological differences.

Nonalcoholic sons of alcoholic fathers have different brain wave patterns. Event-related potentials—electrophysiologic phenomena in the brain associated with sensory stimuli or specific mental processes—have been found to differ significantly in the sons of alcoholic and nonalcoholic fathers. The 30 subjects in the study were normal young men who were moderate social drinkers. Half of the subjects' fathers were judged to be alcoholic based on loss of employment or broken marriage due to excessive drinking. The other half had no family history of alcoholism.

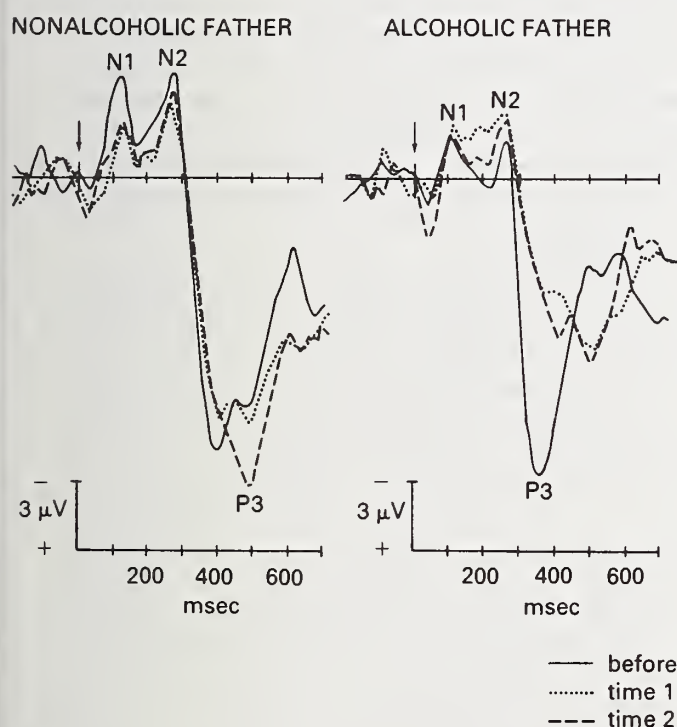


FIGURE 1a. Characteristics of the P3 wave after administration of alcohol. Striking differences were found in the amplitude and shape of the P3 wave in the two kinds of subjects after administration of an alcohol dose (0.56 g/kg body weight). Alcohol produced an immediate and substantial reduction in P3 amplitude in the sons of alcoholic fathers that persisted at least 30 minutes (right side of figure). In contrast, there was only a slight reduction of P3 amplitude in the sons of nonalcoholic fathers.

SOURCE: Elmasian et al. 1982.

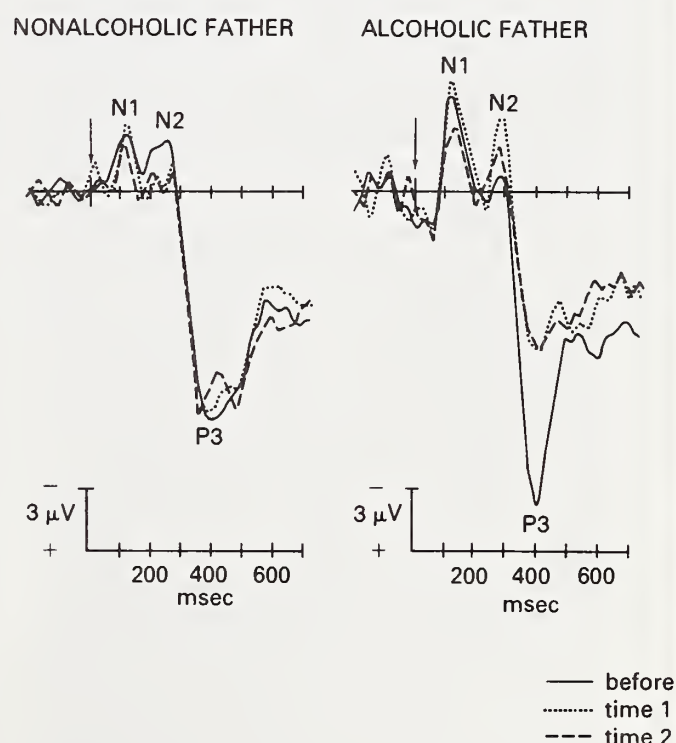


FIGURE 1b. Characteristics of the P3 wave after administration of a placebo. Differences in P3 amplitude response also were found in the sons of alcoholic and nonalcoholic fathers when alcohol was expected but a placebo was administered instead. Mere expectation of receiving alcohol immediately caused a large reduction of P3 amplitude in the sons of alcoholic fathers that persisted at least 30 minutes (right side of figure). Alcohol expectancy produced no significant change in P3 amplitude in the sons of nonalcoholic fathers (left side of figure).

SOURCE: Elmasian et al. 1982.

While ERP characteristics in persons at risk for alcoholism may be a biological marker of a genetic susceptibility to alcoholism, establishing conclusively that this is so will require longitudinal studies in which persons with known ERP patterns would be followed for several years to correlate their early ERP measurements with the drinking patterns they eventually develop.

## NEUROPSYCHOLOGICAL DIFFERENCES

The discovery of brain electrophysiological differences in the sons of alcoholics suggests that neuropsychological differences could also be present in such persons—that the electrical differences might have behavioral correlates. Several studies of male alcoholics have found deficits in neuropsychological functioning (Kleinknecht and Goldstein 1972; Tarter 1975; Parsons 1977). Although these deficits have been interpreted as being consequences of alcoholism, the demonstration of electrophysiological differences in high-risk persons, as discussed earlier, raises the question of whether some neuropsychological deficits may be antecedents of alcoholism as well as genetic markers of susceptibility to it.

Unfortunately, few studies have compared high-risk (family history of alcoholism) and low-risk groups (no such family history) on neuropsychological tasks. Jones-Saumty et al. (1980) reported that family history of alcoholism had no significant effect on women's performance on tests of abstracting ability and intelligence, but this finding could stem from the fact that heredity is a weaker factor in female alcoholism (Goodwin 1979).

Hennecke (1984) compared perceptual characteristics in 30 children of alcoholic fathers and 30 children of nonalcoholic fathers. The children, boys and girls 10 to 12 years old, were given a test that measures a trait called stimulus augmenting, the tendency to perceive a stimulus more strongly than normal. Other studies have found that alcoholics are stimulus augmenters; they perceive stimuli such as pain more strongly than others—that is, they suffer more—and it has been suggested that their drinking could represent an adaptive mechanism to reduce this oversensitivity (Coger et al. 1976; Petrie 1978; Buchsbaum and Ludwig 1980). Hennecke hypothesized that stimulus augmentation may precede the development of alcoholism. There was a significantly higher percentage of stimulus augmentation in the children of alcoholic fathers, suggesting that stimulus augmenting may precede and be predictive of alcoholism. It is not clear from this study, however, whether this situation was due to genetic or environmental factors associated with paternal alcoholism. Hennecke notes that although the current drinking status of the alcoholic father was not significantly correlated to test scores in the children, environmental factors cannot be ruled out as contributors to the observed stimulus augmentation in those children.

In another study, Schaeffer et al. (1984) tested the hypothesis that nonalcoholic men with a family history of alcoholism (alcoholic father, mother, or sibling) would show deficits in neuropsychological performance. The 130

subjects, 24 to 60 years old, consisted of alcoholics and nonalcoholics, and each group included subgroups with and without a family history of alcoholism. The subjects were given a number of tests to measure verbal ability, learning and memory, abstracting and problem solving, and perceptual-motor performance. Nonalcoholics with a family history of alcoholism performed significantly worse on tests of abstracting/problem solving and perceptual motor functioning than did nonalcoholics who had no family history of alcoholism. Although these results are consistent with the hypothesis that some neuropsychological deficits may precede alcoholism in men with a positive family history, they are contradicted by another recent study (Hesselbrock 1983) that found no significant differences between the sons and daughters of alcoholic and control subjects on neuropsychological tests. This discrepancy may have been due to differences in the age of subjects and other methodological differences between the two studies.

Cognitive deficits were found in a recent neuropsychological assessment of young men who are sons of alcoholic fathers and therefore at risk of alcoholism (Drejer et al. 1985). The assessment, part of a long-term prospective study of risk factors for alcoholism under way in Denmark, involved 204 males, 18 to 19 years old, of whom 134 are the sons of alcoholics. The other 70 subjects constitute a control group matched for several social and familial variables. Because alcohol consumption was essentially equal in the two groups, comparable to that of other Danish males in this age group, and not yet heavy because of the young age of the subjects, it was considered unlikely that any differences in cognitive functioning could be due to alcoholism.

The subjects were administered a neuropsychological test battery that measured general intelligence (including vocabulary), memory, attention, field dependence (ability to identify a simple figure hidden in a complex printed design), categorizing ability, and organizing and planning. Although there were more similarities than differences between the two groups, the high-risk group had a significantly poorer vocabulary and performed significantly worse on tests of categorizing ability and organization/planning. Analysis of error patterns in the categorizing test suggested that the high-risk group has a reduced capacity for sustained goal-directed activity, and that one way this reduced capacity is manifested is by a rigid, inflexible approach to problem solving. This trait was also detected in analysis of data from the organization/planning test, which indicated an impulsive aspect to problem-solving behavior in the high-risk group. Interestingly, these tests showing poor vocabulary and impulsiveness among members of the high-risk group were consistent with evaluations provided by their schoolteachers in response to questionnaires (Knop et al. 1985).

These cognitive deficits in nonalcoholic young men at risk for alcoholism may well be markers of a genetic predisposition to alcoholism, although, again, environmental factors associated with having an alcoholic father have not been ruled out as an alternative explanation for



these deficits. Drejer and her colleagues suggest, however, that even if these cognitive deficits turn out not to have a genetic origin, they might still predispose to alcoholism. Difficulties in control and regulation in cognition, they suggest, will probably lead to more psychosocial stress in the future in these subjects.

Recently Hegedus et al. (1984) examined static ataxia as a possible neurological marker of genetic predisposition to alcoholism. Static ataxia is a tendency of the upper body to sway when an individual is standing. The research was inspired by previous work by Lipscomb et al. (1979), who found that nonalcoholic young adults who had an alcoholic relative showed more upper body sway than subjects without an alcoholic relative. Hegedus et al. confirmed and extended this earlier work by clearly establishing an alcoholism diagnosis in the relatives and verifying the degree of their relatedness to the subjects. The investigators compared 20 sons of alcoholic fathers, 22 sons whose fathers suffered from depression, and 15 controls whose fathers had neither of these conditions. None of the subjects had a history of alcohol abuse, drug abuse, psychiatric disturbance, mental retardation, or neurological disorder. Measurements of upper body sway showed no difference between the controls and the sons of depressed fathers, but the sons of alcoholic men had significantly more static ataxia than either of the two other groups. These differences occurred only when the subjects were measured with their eyes open; static ataxia was the same in all three groups when the measurements were made with the subjects blindfolded.

Hegedus and her colleagues suggested that increased upper body sway in the sons of alcoholic men may be a neurological expression of genetic predisposition to alcoholism. Again, however, environmental causes could not be ruled out: the investigators also suggested that, alternatively, the increased static ataxia might be "an acquired neurological pathology consequential to living with an alcoholic father" (Hegedus et al. 1984). Thus, although this study points to excess upper body sway as a possible risk factor for alcoholism, it does not settle the question of whether its origin is genetic or environmental.

In summary, the state of knowledge at this time concerning neuropsychological deficits as markers of genetic predisposition to alcoholism is not well developed. There seems to be a link between alcoholism in a parent and certain neurobehavioral characteristics in offspring, but environmental causes for such a link have not been ruled out. The question raised at the beginning of this section—whether brain electrical anomalies in high-risk sons of alcoholics have behavioral correlates that can also serve as genetic markers of susceptibility—is still open.

## BIOCHEMICAL DIFFERENCES

Most alcohol metabolism in mammals occurs in the liver. The liver enzyme system that is responsible for most alcohol elimination consists of two enzymes—alcohol dehydrogenase (ADH), which converts ethanol to acetal-

dehyde, and aldehyde dehydrogenase (ALDH), which converts acetaldehyde to acetate for final oxidation to carbon dioxide and water. ADH is the rate-limiting enzyme in this system. Two other liver enzyme systems, the microsomal ethanol oxidizing system (MEOS) and the catalase system, also metabolize alcohol, but to a lesser extent than the ADH system.

Much genetic variation has been found in the molecular structure and catalytic properties of ADH and ALDH, as emphasized in two recent reviews (Bosron and Li 1986; Li and Bosron 1986), and much attention has been focused on these enzymes to explain why there can be great differences in alcohol elimination rates among individuals, ethnic groups, and races. Individuals can vary twofold to threefold in their ability to eliminate alcohol (Bennion and Li 1976; Kopun and Propping 1977; Keiding et al. 1983), and it has been estimated that heredity explains at least 50 percent of the variance of ethanol metabolic rates (Kopun and Propping 1977). A more recent estimate, based on studies of twins (discussed in the next paragraph), is that 62 percent of the variability in peak blood alcohol concentration and 49 percent of the variability in alcohol elimination rate are genetically determined (Martin et al. 1985).

A prominent hypothesis is that, in addition to environmental factors such as diet, chronicity of alcohol consumption, and smoking, variations in the rate of alcohol metabolism are determined by the particular combinations of variant forms of these enzymes that people inherit. A genetic basis for variation in alcohol elimination rate is indicated by a recent study of twins, for example. Martin et al. (1985) administered alcohol to 206 monozygotic (identical) and dizygotic (fraternal) twins to determine the effect of genetic factors on peak blood alcohol concentration, the time it took to reach that concentration, and the alcohol elimination rate. A genetic influence was indicated by the fact that identical twins showed significantly less variance on these measurements than fraternal twins. Other evidence has come from comparisons of alcohol elimination rate between Asian and European populations. Hanna (1978) reported that the mean alcohol elimination rates in Japanese and Chinese populations, who have a high frequency of a very active form of ADH, are about 30 percent higher than in Europeans, who have a low frequency of this type of ADH. Studies to directly compare alcohol elimination rates in persons with known ADH genotype have not been done because a noninvasive method for determining these genetic variants has yet to be developed (Li and Bosron 1986).

As pointed out by Schuckit (1984), however, there is little evidence that the gross rate of alcohol metabolism is itself associated with the risk for alcoholism. Thus, although Goodwin et al. (1974) found that the risk of alcoholism in children adopted from alcoholics was four to five times greater than in controls, they did not differ from controls in the rate of alcohol clearance (Utne et al. 1977). The same conclusion is supported by Schuckit's (1981) studies showing identical rates of disappearance of alcohol in young men with and without alcoholic relatives.



Although there appears to be no direct relationship between the overall rate of alcohol elimination and the risk of developing alcoholism, many investigators still consider it likely that genetic variations in alcohol metabolizing enzymes could, through other mechanisms, cause some individuals to be more susceptible to alcoholism or alcohol-induced disorders than others.

### Acetaldehyde Levels: A Genetic Marker of Susceptibility?

Some studies have focused on the question of whether levels of alcohol-derived acetaldehyde are somehow involved in the genetic susceptibility to alcoholism, because genetic variations in the catalytic efficiency of enzymes that produce and remove acetaldehyde could be expected to affect the levels of this substance in the tissues. Literature on the possible role of acetaldehyde in the genesis of alcoholism has been extensively reviewed by Schuckit (1984).

Acetaldehyde, which is produced by all major systems for metabolizing ethanol, is a highly toxic compound that is believed by some investigators to be a possible cause of several disorders associated with alcoholism. According to classical chemical principles, the level of acetaldehyde in a tissue at any given time is determined by two factors: its rate of formation by ADH or other alcohol-metabolizing enzymes and its rate of removal by ALDH (and other mechanisms). For example, if the rate of formation is fast and the rate of removal is slow, the steady-state level of acetaldehyde should be higher than it would be if the rate of formation were slow and the rate of removal were fast.

Because genetic variants of ADH and ALDH may catalyze the conversion of their respective substrates at different rates, persons who have inherited certain combinations of these enzyme variants may attain higher levels of acetaldehyde than people with other combinations would. It has been hypothesized (Schuckit 1984) that acetaldehyde per se may have some etiological role in the development of alcoholism and that a tendency to produce higher levels of acetaldehyde after alcohol consumption may therefore constitute a genetic marker of predisposition. This idea is controversial, however, because it is not well supported by clear-cut studies.

Three studies have found that alcohol administration caused acetaldehyde levels to rise to substantially higher levels in short-term abstinent alcoholics than in nonalcoholics (Freund and O'Hallaren 1965; Truitt 1971; Korsten et al. 1975), although one study (Lindros et al. 1979) found no such differences between alcoholics and controls. On balance, these studies suggest a probable increase in acetaldehyde in alcoholics, but the measurement of acetaldehyde in biological fluids is fraught with technical difficulties and is subject to significant errors. In any case, the positive studies provide no information as to whether this tendency is antecedent to the development of alcoholism or is a consequence of it.

Evidence that a tendency to overproduce acetaldehyde may precede the development of alcoholism has come from drinking experiments in which acetaldehyde levels in

nonalcoholic men with a family history of alcoholism were compared with levels in nonalcoholic men without such a family history. Over a 5-hour period after receiving 0.75 mL of ethanol per kg body weight, breath acetaldehyde measurements in subjects with a family history of alcoholism were twice as high as in controls (Schuckit and Raynes 1979; Schuckit in press). However, most attempts to replicate these findings and to demonstrate that elevated acetaldehyde after drinking is a genetic marker of susceptibility to alcoholism have not been successful. Indeed, as discussed in the next section, it appears more likely that acetaldehyde elevation is an explanation of genetic aversion to alcohol.

### Genetic Variations in ADH and ALDH

ADH is a highly polymorphic enzyme—that is, it exists in many forms. At least 20 electrophoretically different enzyme forms (isozymes) have been found in humans, and it seems likely that more variants will be discovered. This diversity arises from the fact that more than one gene for the formation of ADH exists in human populations.

ADH consists of two polypeptide subunits. The synthesis of ADH subunits is directed by five different genes designated *adh*<sub>1</sub> to *adh*<sub>5</sub>, each of which directs the synthesis of a specific kind of ADH subunit. Thus, several combinations are possible in a population. Additional variations can arise when mutations occur in the genes that control the synthesis of these subunits. However, all genetic variations discovered so far in human ADH have resulted from mutations in the *adh*<sub>2</sub> and *adh*<sub>3</sub> genes (von Wartburg and Schurch 1968; Harada et al. 1978a, 1980b; Teng et al. 1979; Bosron et al. 1980; Bosron and Li 1981).

Although some of the ADH isozymes differ structurally from each other by only one amino acid, these differences are sufficient to have significant effects on properties of the whole enzyme, including the rate at which alcohol is converted into acetaldehyde. In particular, variants produced by the *adh*<sub>2</sub> gene have widely different kinetic properties (Bosron et al. 1980, 1983; Bosron and Li 1981; Yin et al. 1984).

Polymorphism also exists in ALDH, but to a lesser degree than in ADH. Most investigators agree that there are at least four known isozymes of human liver ALDH (Greenfield and Pietruszko 1977; Harada et al. 1978a; Goedde et al. 1979; Harada et al. 1980a; Teng 1981), and that they differ in the rate at which they convert acetaldehyde to acetate.

In view of this genetic diversity in alcohol metabolizing enzymes, it is not difficult to imagine that one combination of inherited ADH and ALDH isozymes might cause acetaldehyde to rise to higher levels than another combination. ADH and ALDH isozymes have varied distributions in human populations, which may account for racial and ethnic variations in the ability to remove alcohol-derived acetaldehyde as well as for variations in the frequency of a skin-flushing reaction when relatively small quantities of alcohol are consumed. This reaction is common among Orientals, for example, and a prominent hypothesis is that



it is due to greater accumulation of alcohol-derived acetaldehyde resulting from the properties of alcohol-metabolizing enzymes in these populations.

About 80 percent of Orientals have a form of ADH that is found in only 5 to 10 percent of whites, and *in vitro* studies (Ewing et al. 1974; Stamatoyanopoulos et al. 1975; Yin et al. 1984) suggest that the Oriental form produces more rapid conversion of alcohol to acetaldehyde. Unfortunately, efforts to demonstrate similar effects *in vivo* or to show consistent differences in the rate of ethanol metabolism between flushers and nonflushers have been unsuccessful (Edwards and Evans 1967; Bennion and Li 1976; Hanna 1978; Mizoi et al. 1979). Future research may demonstrate greater frequency of certain ADHs in alcoholics than in controls.

In contrast to ADH, excellent correlations have been found between genetic variations in aldehyde dehydrogenase and observed population differences in the prevalence of the flushing reaction and, possibly, of alcoholism. Studies have shown that populations differ in the prevalence of ALDH isozymes with varied affinity for the substrate, acetaldehyde. Studies by Harada et al. (1978b, 1979) indicate that Westerners have two predominant ALDH isozymes that differ in their affinity for acetaldehyde: a high-affinity type found in mitochondria (a type of subcellular structure) and a low-affinity type found in the cytosol (cellular fluid). These high- and low-affinity forms of ALDH were found in 100 percent of a population of Germans, whereas 52 percent of a Japanese population had only the low-affinity isozyme. Because there is evidence that facial flushing after alcohol consumption is correlated with the absence of the high-affinity (i.e., more efficient) form of ALDH called the ALDH<sub>2</sub> isozyme (Goedde et al. 1980; Inoue et al. 1980), the facial flushing so common in Orientals may be due to a greater accumulation of acetaldehyde (Mizoi et al. 1979).

Immunological tests on Orientals who have the flushing reaction have shown that the ALDH<sub>2</sub> enzyme protein is present but in a catalytically inactive form. This inactive variant is found in about 40 to 50 percent of Japanese, 35 percent of Chinese, and more than 40 percent of Vietnamese and Indonesians (Goedde et al. 1983). Another variant ALDH, possibly arising from a mutation in the ALDH<sub>1</sub> gene, has been found in some Orientals (Yoshida et al. 1983), but its frequency could not be determined because of the small number of liver samples that were examined.

It has been hypothesized that the discomfort of the flushing reaction and associated symptoms—hot skin, fast pulse—may provide many Orientals with a “built-in” deterrent to excessive drinking, and that this might explain the lower prevalence of alcoholism among Orientals. Several lines of evidence support this idea. The flushing reaction also occurs when recovering alcoholics using the deterrent drug disulfiram (Antabuse) take a drink. Disulfiram, a potent inhibitor of ALDH, causes acetaldehyde concentrations to rise and produce discomfort, thus deterring further drinking. Also consistent with the built-in deterrence hypothesis is a report that, along with the flushing reaction, Japanese individuals deficient in ALDH<sub>2</sub>

activity achieve very high blood acetaldehyde levels after consuming the equivalent of about an ounce of pure alcohol (about one and one-half drinks), although their overall rate of alcohol metabolism is about the same as that of persons with normal ALDH<sub>2</sub>. Finally, a study by Harada et al. (1982) found that the prevalence of the inactive ALDH<sub>2</sub> is lower among Japanese alcoholics than among the general Japanese population. This finding suggests that high acetaldehyde accumulation after drinking, and the flushing reaction this causes, also may be less prevalent among Japanese alcoholics. Thus, they may lack the built-in deterrence to alcohol abuse provided by the flushing reaction.

The observed accumulation of highly toxic acetaldehyde in people who are genetically deficient in functional ALDH<sub>2</sub> has led to speculation (Bosron and Li 1986; Li and Bosron 1986) about what might happen to people with genetically impaired ability to remove acetaldehyde if they drink heavily despite the flushing reaction. The higher accumulation of acetaldehyde in such people might make them more susceptible to liver and brain damage. Both of these consequences of alcohol abuse and alcoholism are known to be influenced by genetic factors (von Wartburg and Buhler 1984), and it may be that the tendency of certain inherited forms of alcohol-metabolizing enzymes to yield higher levels of acetaldehyde is an underlying mechanism of genetic influence on these alcohol-related pathologies.

Good progress is being made in clarifying the role that genetic variation of alcohol-metabolizing enzymes may have in determining susceptibility to alcoholism and alcohol-related pathologies. However, future progress will depend greatly on the development of improved methods for measuring acetaldehyde (Eriksson 1980, 1983; Lindros 1983; Fukunaga et al. 1986). Assays for this compound are technically difficult and controversial. Among the problems are loss of acetaldehyde during preparation of the sample, spurious production of acetaldehyde by reagents used to remove protein from the sample, and uneven distribution of acetaldehyde in the tissues, making it difficult to generalize from blood or breath samples.

### Low Monoamine Oxidase Levels as a Possible Genetic Marker

Monoamine oxidase (MAO), an enzyme involved in brain neurotransmitter metabolism but also found in blood platelets, has been reported in several studies to be abnormally low in alcoholics (Gottfries et al. 1975; Takahashi et al. 1976; Brown 1977; Wiberg et al. 1977; Major and Murphy 1978; Sullivan et al. 1978, 1979; Orelund 1983; Orelund et al. 1983, 1985; Shaskan 1983). These studies have ranged from clinical and case-control approaches to population and family surveys, but, despite differences in study design, all have reported lower platelet levels of MAO in alcoholics than in controls.

Other research indicates that MAO activities are under strong genetic control (Fowler et al. 1982). This research, together with the frequent observation of low MAO levels in alcoholics, has led to a hypothesis that the low MAO



levels may be antecedent to the development of alcoholism, that is, a biochemical marker of genetic susceptibility (Buchsbaum et al. 1976).

One study of platelet MAO levels examined nonalcoholic college students and their parents (Puchall et al. 1980). The investigators found that the subjects who had lower MAO levels tended to have parents who also had low MAO levels, and that the association was statistically significant. The prevalence of alcoholism among the parents of the low MAO probands was also significantly greater than among parents of high MAO probands, making it unlikely that alcohol causes the low MAO levels frequently found among alcoholics. Data from other studies (Wiberg et al. 1977; Major and Murphy 1978; Sullivan et al. 1978, 1979; Shaskan 1983) support the same conclusion.

### MAO Activity in Alcoholics with Milieu-Limited and Male-Limited Genetic Susceptibility

Differences in MAO activity have recently been found in alcoholics with two different kinds of inherited predisposition to alcoholism. As discussed earlier in this chapter, studies of adoptees in Sweden have identified two types of genetic predisposition to alcoholism: milieu-limited and male-limited. Milieu-limited susceptibility occurred in both sexes, was transmissible by either biological parent, and required environmental provocation to become expressed as alcoholism in the children. The alcoholism in those biological parents had a late onset, was usually not severe, and was associated with minor encounters with law enforcement agencies. Male-limited susceptibility occurred only in males, was highly heritable, gave rise to severe early-onset alcoholism requiring extensive treatment in the biological fathers, and was associated with serious law-breaking by those fathers. These predispositions were identified by studying data from official records, not by conducting clinical examinations.

The first confirmation of this typology in a clinical setting was recently published by von Knorring et al. (1985). Although this is significant in itself, the investigators also found that the two types of alcoholism were separable by platelet MAO activity.

The study population consisted of 36 alcoholics (31 men and 5 women) treated in an outpatient department of a university hospital, compared with 34 controls with no history of drinking problems either personally or among first-degree relatives. Diagnosis of alcoholism was by standard criteria (Diagnostic and Statistical Manual, Third Edition). After diagnosis, subjects were classified as either milieu-limited or male-limited alcoholics on the basis of age of onset, severity of alcoholism and its social consequences (e.g., family and job difficulties), frequency and seriousness of legal difficulties arising from alcohol abuse (e.g., arrests for fighting and traffic accidents), and family history.

Measurement of platelet MAO levels revealed significant differences between the two groups of alcoholics. Male-limited alcoholics had significantly lower platelet MAO activities than milieu-limited alcoholics and healthy

controls, but there were no significant differences between milieu-limited alcoholics and controls (figure 2).

This research is important for two reasons: it is the first clinical confirmation of the alcoholism typology identified in the Swedish adoption study by examination of records, and it indicates that biochemical characteristics may become useful for distinguishing subtypes of alcoholism and identifying individuals at risk.

These findings need to be replicated by other investigators, but they are most encouraging.

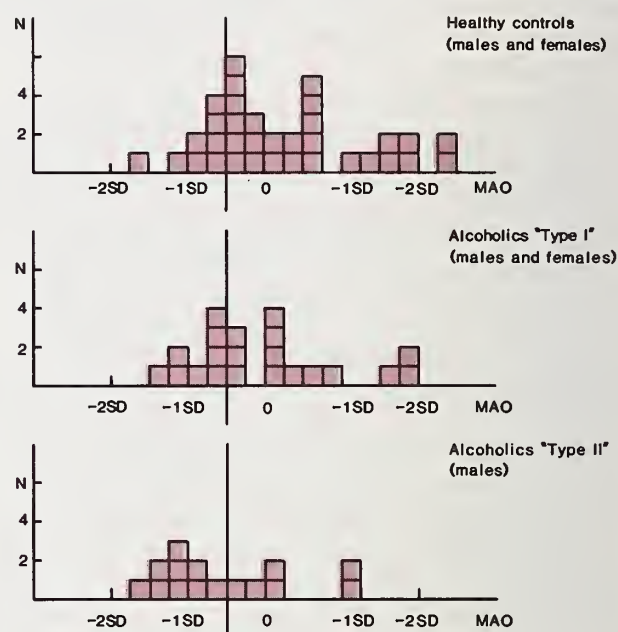


FIGURE 2. Platelet monoamine oxidase (MAO) activity in healthy controls, milieu-limited alcoholics (Type I alcoholism), and male-limited alcoholics (Type II alcoholism). Values on the horizontal axis are standard deviations from the mean (normal) value of platelet MAO. The vertical axis is the number of individuals showing a given deviation from the mean. The distribution of MAO activities is essentially the same in the controls and the milieu-limited alcoholics, but the distribution of MAO activities is at significantly reduced levels in the male-limited alcoholics.

SOURCE: von Knorring et al. 1985.

### SUMMARY

Evidence for genetic predisposition to alcoholism continues to grow. It is now widely accepted by researchers in the field that alcoholism can result from the interaction of heredity and environment. The evidence for genetic factors includes data from studies of familial alcoholism, studies of twins, studies of adoptees separated from their biological parents at an early age, and animal-breeding experiments.

Studies of adoptees in Sweden have identified two types of genetic predisposition to alcoholism: milieu-limited and male-limited. Milieu-limited susceptibility occurred in both sexes and required environmental provocation to become



expressed as alcoholism. The alcoholism had a late onset in the biological parents, was usually not severe, and was associated with minor encounters with law enforcement agencies. Male-limited susceptibility occurred only in the biological fathers of the adoptees, was highly heritable, gave rise to severe early-onset alcoholism often requiring extensive treatment, and was associated with serious law-breaking. These predispositions were identified by studying data from official records, not by conducting clinical examinations.

Researchers are seeking to identify neurophysiological, neuropsychological, and biochemical markers of genetic susceptibility to alcoholism and to understand how such alterations might be involved in mechanisms that lead to alcoholism. Identification of such markers could also have important implications for the prevention of alcoholism.

Characteristic brain electrical patterns have been found in subjects who are not alcoholic but are judged to be at high risk for alcoholism because alcoholism exists among their first-degree relatives, particularly their fathers. Fast electroencephalographic activity and deficiencies in alpha, theta, and delta EEG activity have been reported in the high-risk sons of alcoholics. Experiments in which alcohol was administered to such subjects found greater alterations in alpha wave activity than in controls.

Studies of event-related potentials in the nonalcoholic sons of alcoholic fathers have revealed a decreased amplitude in the P3 wave similar to that found in abstinent alcoholics. The evidence suggests that decreased P3 amplitude precedes the development of alcoholism and may be a genetic marker of susceptibility.

Presumably, altered brain electrophysiology could have psychological correlates that could also be markers of susceptibility. There have been few studies of neuropsychological performance in high-risk groups, however. Tests of abstracting/problem solving, perceptual-motor functioning, and stimulus augmenting have shown poorer performance in nonalcoholic men with a family history of alcoholism than in controls without a family history of alcoholism. Although these might be related somehow to genetically based alterations in brain functioning, environmental causes for these differences have not been ruled out.

Considerable progress is being made in the area of biochemical markers of genetic predisposition to alcoholism and its associated disorders, and plausible hypotheses have emerged from some highly intriguing research. Much research on genetic markers of susceptibility is focused on genetic variation in alcohol-metabolizing enzymes, especially on how such genetic variations could affect tissue levels of acetaldehyde, the first metabolic product of alcohol. Elevated acetaldehyde levels have been implicated as the cause of the dysphoric alcohol flush reaction that is very common in Orientals. The reaction appears to be correlated with the absence of a high-activity form of aldehyde dehydrogenase, which is noted in up to 50 percent of Oriental populations but almost never in Western populations. It is hypothesized that higher acetalde-

hyde, and the uncomfortable flushing reaction it can cause, provides protection against excessive drinking and that this may account for lower alcoholism rates among Orientals.

Another potential biochemical marker of genetic susceptibility to alcoholism is low levels of platelet monoamine oxidase. Studies have shown that alcoholics and their nonalcoholic children both tend to have lower levels of this enzyme. The probability that monoamine oxidase is a genetic marker of susceptibility to at least one type of alcoholism has been greatly increased by a recent clinical study that examined levels of this enzyme in alcoholics diagnosed as having either milieu-limited or male-limited alcoholism on the basis of criteria defined by the Swedish adoption studies. The male-limited alcoholics had significantly lower levels of platelet monoamine oxidase. This is the first clinical validation of these two types of genetic predisposition to alcoholism. It also indicates that low monoamine oxidase levels are a genetic marker of susceptibility to male-limited alcoholism, a severe form of the disease, and that monoamine oxidase assay may allow early identification of individuals with that susceptibility. If these findings can be replicated, the implications for prevention and treatment are significant.

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# Psychobiological Effects of Alcohol

The brain is a major target for the actions of alcohol. Alcohol's effects are reflected first in neurochemical alterations, psychological and behavioral (functional) deficits, and subsequently in histological (structural) alterations. Since the publication of the *Fifth Special Report to the U.S. Congress on Alcohol and Health* (USDHHS 1984), advances have been made in research on alcohol's effects at the level of the nerve cell (neuronal) membrane; the mechanisms underlying intoxication, alcohol tolerance, and physical dependence; and possible correlations between alcohol-induced structural and functional brain changes. These key studies are the primary focus of this chapter.

## ACUTE ALCOHOL EFFECTS

### The Neuronal Membrane

The neuronal membrane is the place where biochemical effects of alcohol on the central nervous system (CNS) begin. Neuronal membranes are heterogeneous mixtures of lipids and proteins surrounding a cell. The lipids, primarily phospholipids, are arranged in a bilayer. Within this lipid matrix are inserted the various functional proteins that mediate the conduction and transmission of information in the CNS (Tabakoff and Hoffman in press) (see figure 1).

The membrane can be very ordered, with minimal movement of molecules within it, or quite fluid, with considerable movement possible. Alcohol-induced changes in fluidity, or the mobility of molecules within brain membranes, are an important field of research today (Hunt 1985).

Alcohol is generally thought to disrupt normal membrane function by penetrating into the membrane. Within the membrane, alcohol expands the volume of the mem-

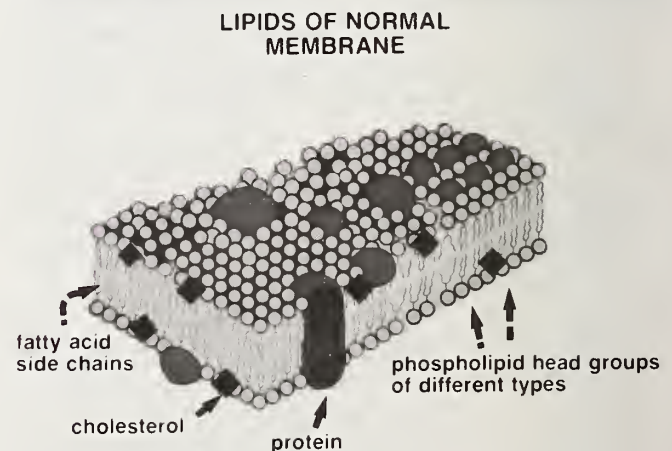


FIGURE 1. An artist's rendition of a portion of a neuronal membrane. The membrane is composed of various lipids, primarily phospholipids, which are arranged in a bilayer. Within this lipid matrix are inserted the various functional proteins that mediate the conduction and transmission of information in the nervous system.

Provided by Dr. Boris Tabakoff.



brane and disorders the lipid components. Alcohol may interact directly with membrane proteins as well, but the evidence is not conclusive (Hunt 1985). The acute intoxicating actions of alcohol may be mediated by its perturbation of membrane lipids and the subsequent alteration in the function of membrane proteins (see figure 2).

Recent research indicates significant specificity of the actions of alcohol at the molecular level (Tabakoff and Hoffman in press). Alcohol is not distributed diffusely throughout membranes but may occupy a particular membrane region, thereby producing very selective effects.

Reexamination of alcohol's effects on the fluidity of neuronal membranes obtained from long-sleep (LS) and short-sleep (SS) mice, inbred rodents with different sensitivity to alcohol's acute hypnotic and depressant effects, revealed a difference between these lines with the use of electron paramagnetic resonance but not fluorescence polarization (Perlman and Goldstein 1984). Because these two physical-chemical techniques monitor different membrane regions, the findings suggest that the main site affected by genetic selection—that is, the site that influences the hypnotic response to alcohol—is probably localized within a restricted area of the neuronal membrane. A recent study (Kreishman et al. 1985) suggests that nuclear magnetic resonance has the potential to provide even better examination of alcohol-induced lipid perturbation than either of the aforementioned physical chemical techniques.

### Electrical Conduction

Alcohol's membrane-disordering effect can be quite small, yet this minor effect can grow into a larger one involving a functional physiological mechanism such as ion flux (Hunt 1985). The mechanism underlying neuronal electrical activity is the ability of ions to flow through neuronal membranes in a precise manner in response to proper stimuli. This topic is discussed extensively in the *Fifth Special Report* (USDHHS 1984). An alcohol-induced

#### EFFECT OF ALCOHOL ON NORMAL MEMBRANE

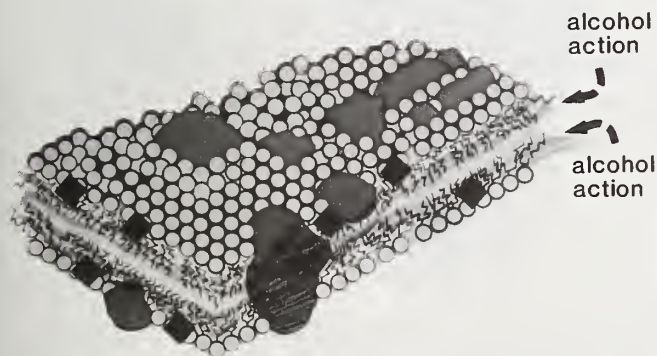


FIGURE 2. The effect of alcohol on normal membrane. It is thought that the acute intoxicating actions of alcohol are mediated by the perturbation of membrane lipids and the subsequent alteration in the function of membrane proteins.

Provided by Dr. Boris Tabakoff.

change in the microenvironment of a membrane can have profound effects on neurotransmission, the signaling that occurs within and between neurons. The rodent hippocampus, cerebellum, and the locus coeruleus (LC), a brain structure whose neurons project into many areas of the brain and spinal cord, have been useful models for studying the effects of alcohol on the electrical properties of membranes.

The differential sensitivity of the various brain areas appears to be influenced genetically. The differential sensitivity of LS and SS mice to alcohol's sedative effects has been correlated to the sensitivity to alcohol of the Purkinje cell layer of the cerebellum (Basile et al. 1983). A recent study (Johnson et al. 1985) of two inbred rat strains has shown that the association between Purkinje cell sensitivity and sedative effects of alcohol can be generalized to rats. Alcohol applied locally to neurons was significantly more potent in reducing neuronal firing rates in Fischer 344 rats than in Brown Norway rats, and alcohol's hypnotic effect lasted significantly longer in the Fischer strain.

Purkinje cells are only one locus for generating alcohol's different behavioral effects in LS and SS mice. Large differences between alcohol-induced sleep times have been found in LS and SS mice with the cerebellum removed, suggesting that neuron populations in other brain regions also possess differential sensitivities to the depressant effects of alcohol in these mouse strains (Palmer et al. 1984).

The basal firing rate of rat LC neurons also has been found to affect the sensitivity of these neurons to alcohol. Electrophysiological research using recording outside the cells has shown that alcohol decreases spontaneous firing in some LC neurons in vivo (Pohorecky and Brick 1977; Strahlendorf and Strahlendorf 1983) and sensory-evoked firing in LC neurons (Aston-Jones et al. 1982). In a rat brain slice preparation, very low alcohol concentrations have been found to have variable effects on firing rate: the firing rate of most LC neurons was inhibited, while the firing rate of other LC neurons remained unaffected or even increased. In contrast, higher alcohol concentrations (similar to those found in the rodent brain during behavioral states ranging from mild intoxication to sedation) consistently inhibited neuronal firing (Shefner and Tabakoff 1985). This biphasic alcohol effect resembles the biphasic action on turnover of the neurotransmitter norepinephrine when alcohol is injected into intact rats (Aragon et al. 1984).

### Neuroreceptor Systems

Because neurotransmitters transfer information from one neuron to another by interacting with appropriate receptors on the surface of postsynaptic neurons, a functional effect of alcohol's capacity to disrupt neuronal membrane structure may be a disruption of the flow of information within the brain. Specifically, alcohol may prevent the information that is transmitted between neurons from being translated into electrical impulses (Hunt 1985). It is the function of receptors to recognize the chemical message and "unlock" the membrane of the receiving neuron to permit the signal to continue (USDHHS 1984).



Receptors are one component of neuronal membrane proteins. Alcohol has differential effects on particular receptor systems as it does on particular brain regions (Hoffman and Tabakoff 1985). One receptor system specifically affected by alcohol is the gamma-aminobutyric acid (GABA)-benzodiazepine (BDZ) receptor-chloride channel complex. GABA is the main inhibitory neurotransmitter in the brain. BDZs are tranquilizers that, like alcohol, possess anxiolytic (anxiety-reducing) and sedative/hypnotic activity, and that exert their major pharmacologic effects by augmenting the actions of GABA. Both the GABA and BDZ receptors interact with a chloride ( $\text{Cl}^-$ ) channel, apparently represented by a picrotoxinin binding site (Olsen 1981) (see figures 3 and 4).

Suzdak et al. (1986) studied the effects of alcohol on  $\text{Cl}^-$  uptake or binding using a subcellular brain preparation containing a GABA/barbiturate receptor-sensitive  $\text{Cl}^-$  channel system. Barbiturates possess similar anxiolytic and sedative/hypnotic activity as BDZs and augment GABA's actions. Like barbiturates, alcohol stimulates  $\text{Cl}^-$  uptake into brain vesicles at acute intoxicating concentrations. This ability of alcohol to affect  $\text{Cl}^-$  channels provides a mechanism for the common psychopharmacologic actions of alcohol, barbiturates, and BDZs. These investigators conducted another study (Suzdak et al. submitted) to determine whether this mechanism might explain alcohol's ability to produce behavioral intoxication. The ability of different types of alcohols to stimulate GABA receptor-mediated  $\text{Cl}^-$  uptake in brain vesicles was correlated with their intoxication potencies in rats. Excellent correlations were observed between the  $\text{Cl}^-$ -stimulating potencies of

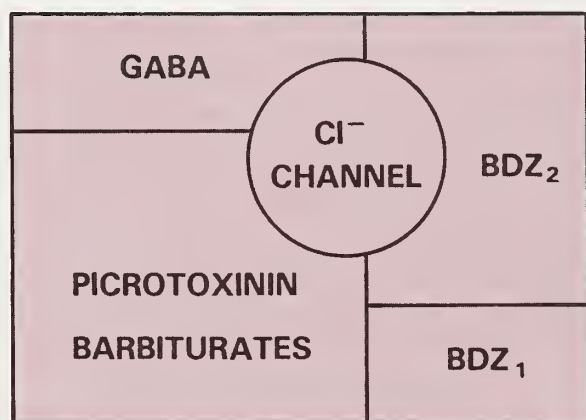


FIGURE 3. Diagrammatic representation of the GABA-BDZ-chloride ionophore receptor complex. The complex appears to be composed of several receptors and subtypes which are characterized by the specific binding of certain radioligands. In some cases the receptors in this complex are linked to the chloride channel, but not always. In addition, the receptors appear to be linked, whereby an action on one has an effect on the activity of another.

SOURCE: Hunt 1983, modified from Olsen 1981.

the tested alcohols and their behavioral potencies as intoxicants. These findings suggest that the ability of alcohols to stimulate membrane  $\text{Cl}^-$  conduction may be related to a specific alteration in the membrane microenvironment of the GABA receptor-coupled ion channel.

Alcohol also may exert some of its actions on membranes through enzymes embedded in them. Enzymes, another component of neuronal membrane proteins, catalyze chemical reactions. One membrane-bound enzyme, adenylate cyclase, is coupled to various CNS neurotransmitter receptors and plays a role in synaptic transmission (Tabakoff and Hoffman in press). Alcohol activates adenylate cyclase differently in different brain regions (Rabin and Molinoff 1981, 1983; Luthin and Tabakoff 1984; Tabakoff et al. 1984; Saito et al. 1985). The adenylate cyclase receptor-coupled system (see figure 4) catalyzes and enhances the synthesis of the chemical cyclic adenosine monophosphate (cAMP) (Needham and Houslay 1982; Luthin and Tabakoff 1984). The cAMP is called a second messenger because it carries a message from the receptors to the interior of the receiving neuron (USDHHS 1984), and the fidelity of these messages may be altered by ethanol.

Calcium ions ( $\text{Ca}^{++}$ ), also referred to as second messengers, regulate neurotransmitter release as well as neurotransmitter actions at receptors. Relatively low doses of alcohol administered acutely can increase  $\text{Ca}^{++}$  uptake in mouse brain preparations, and this action may be related to some of alcohol's acute sedative effects. Studies of  $\text{Ca}^{++}$  metabolism have also indicated the possible biphasic nature of alcohol's acute effects on neurochemical systems (Hoffman and Tabakoff 1985). Recent studies also suggest that acute and chronic alcohol administration can affect  $\text{Ca}^{++}$  metabolism by altering transmitter-stimulated metabolism of phosphatidyl inositides, which are involved in the release of intracellular  $\text{Ca}^{++}$  from membranes (Gonzales et al. 1986; Hoffman et al. 1986).

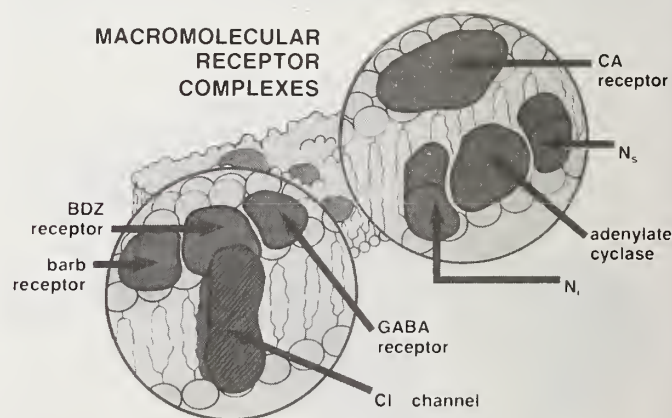


FIGURE 4. Some of the receptor systems that reside in the membranes. Two of the receptor systems that have been investigated extensively are the beta receptor-coupled adenylate cyclase system and the GABA-receptor benzodiazepine receptor-chloride channel complex.

Provided by Dr. Boris Tabakoff.



## CHRONIC ALCOHOL EFFECTS

Chronic alcohol effects can be classified as adaptive (tolerance), maladaptive (physical dependence), or non-adaptive (alcohol-induced organic brain damage). Alcohol's chronic actions on membranes are difficult to interpret because in many cases it is impossible at this level to distinguish between the development of tolerance, physical dependence, alcohol withdrawal syndrome, and brain damage (Hunt 1985).

### Tolerance, Reinforcement, and Physical Dependence

Chronic consumption of alcohol is thought to result in an adaptation within the neuronal membrane. The membranes seem to change their chemical structure so that they can resist the perturbing effects of alcohol—that is, the membrane becomes tolerant to the effects of alcohol (see figure 5). Physiologically, alcohol tolerance refers to a progressive decrease in the sensitivity of an organism to a given dose or concentration of alcohol with repeated use (Hunt 1985). Resistance to the effects of alcohol can manifest itself as environment-independent tolerance to alcohol. This tolerance is unrelated to learning and can be demonstrated regardless of the testing environment. On the other hand, tolerance produced in association with environmental cues (signals that induce a learned response related to the administration of alcohol) is referred to as environment-dependent, conditioned, or learned tolerance (Crowell et al. 1981; Tabakoff 1983; Melchior and Tabakoff 1984). Chronic tolerance can be characterized further as metabolic (pharmacokinetic) or functional (pharmacodynamic). Metabolic tolerance refers to changes in absorption, distribution, degradation, or excretion of alcohol; it is

distribution, degradation, or excretion of alcohol; it is usually exemplified by a change in the duration of alcohol's effect. Functional tolerance is defined as resistance to the effects of alcohol at the cellular level. Its presence is demonstrated when a decreased alcohol effect occurs in the alcohol-tolerant person, as compared with the alcohol-naïve person, at the same cellular (or circulating) level of alcohol (Tabakoff et al. 1986).

Evidence for Pavlovian conditioning in the development of alcohol tolerance in rodents has been demonstrated since the late 1970s, but this finding has only recently been extended to humans (Shapiro and Nathan 1986). Subjects who had received alcohol previously in a "home" environment were tested on a cognitive task under the influence of alcohol in the home environment and in a "distinct" environment. Testing in the presence of cues never before associated with alcohol administration caused poorer performance in the distinct environment than in the home environment.

Findings from animal studies (LeBlanc et al. 1975; Kalant et al. 1978) that acute tolerance to alcohol can develop rapidly led Wilson et al. (1984) to investigate the possibility of demonstrating acute behavioral tolerance to alcohol in humans. They administered two doses of alcohol to 24 brother-pairs and placebo doses to 5 other brother-pairs (controls). The first dose was calculated to result in a peak blood alcohol concentration (BAC) of 100 mg of alcohol per 100 mL of blood (100 mg/100 mL). The second dose was given when the BAC had dropped to half the peak BAC resulting from dose 1, in an attempt to raise the BAC to 100 mg/100 mL. Behavioral test data revealed a consistent decrement in nearly all mean scores after alcohol ingestion, indicating sensitivity to alcohol. Acute behavioral tolerance to alcohol was indicated for some tests by improved performance after dose 2 compared with performance at a time after dose 1 when BACs were approximately the same. Although this study demonstrated that tolerance to certain effects of alcohol develops rapidly, no definitive conclusions were formed about genetic components of sensitivity and acute behavioral tolerance to alcohol.

The development and maintenance of tolerance to the various behavioral and physiological effects of ethanol may involve changes in the function of specific neurochemical systems. Hoffman and Tabakoff (1984) studied the ability of the pituitary hormone arginine vasopressin and structurally related peptides to maintain functional tolerance to alcohol-induced incoordination (ataxia) in mice. They found that these peptides delayed the disappearance of functional tolerance following discontinuation of alcohol exposure, supporting the theory that such peptide hormones modulate a mechanism that maintains alcohol tolerance.

Findings from a recent study (Newlin 1985a) suggest that a certain kind of response to environmental cues associated with alcohol may be a factor in the promotion of environment-dependent tolerance, craving, and withdrawal. In this response, called the antagonistic placebo response, individuals presented with environmental cues

MEMBRANE ADAPTED TO  
PRESENCE OF ALCOHOL  
i.e. Tolerant

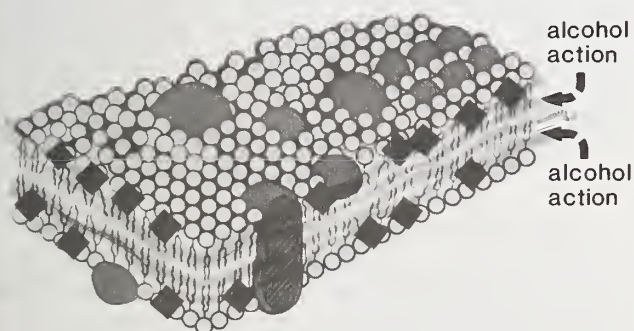


FIGURE 5. Alcohol-tolerant membrane. Chronic consumption of alcohol is thought to result in an adaptation within the neuronal membrane. The membranes are thought to change their *chemical structure* such that they can resist the perturbing effects of alcohol. That is, the membranes become tolerant to the effects of alcohol.

Provided by Dr. Boris Tabakoff.



previously associated with alcohol consumption will experience physiological and psychological responses that are the opposite of those produced by alcohol. For example, an individual who has learned to associate alcohol with relaxation may experience the opposite sensation—*anxiety*—when the environmental cues for alcohol consumption are present but the alcohol is missing or if it is not present in sufficient quantity to produce the desired relaxation. If alcohol cues are present but alcohol is not, the antagonistic placebo response may trigger the desire for alcohol. Furthermore, the antagonistic placebo response may partly nullify the effect of alcohol so that more of it is required to achieve the desired effect. Offspring of alcoholics appear to be prone to develop an antagonistic placebo response, and this response may be associated with familial risk for alcoholism (Newlin 1985b) (see chapter II).

It is generally assumed that alcohol is consumed voluntarily for its pharmacologic effects and that some of these effects are reinforcing and will maintain alcohol consumption (Tabakoff and Hoffman in press). Some of the most exciting research to date on the modulation of alcohol reinforcement has focused on neurons that contain serotonin. Zimelidine, a drug that blocks serotonin uptake by neurons, has been found to reduce alcohol intake by animals in a free-choice situation (Rockman et al. 1979) as well as in human heavy drinkers (Naranjo et al. 1984). The use of serotonergic drugs in lines of rats with differing alcohol preference may provide further evidence for the important role of serotonergic systems in alcohol-induced reinforcement (Murphy et al. 1985).

Physical dependence—as distinct from tolerance and reinforcement—is a state in which a series of withdrawal signs and symptoms are manifested following the abrupt cessation of chronic alcohol intake (as reviewed by Hunt 1985). Less progress has been made in determining the neurochemical systems responsible for physical dependence and alcohol withdrawal symptoms than in identifying the mechanisms underlying tolerance and reinforcement (Tabakoff and Hoffman in press). Research with lines of mice bred selectively for their different sensitivities to alcohol withdrawal—withdrawal seizure-prone and withdrawal seizure-resistant mice—has shown that these mice differ only in sensitivity to alcohol withdrawal seizures and not to generalized seizures produced by other drugs (McSwigan et al. 1984), thereby indicating a genetic basis for susceptibility to the development of alcohol withdrawal seizures. Specific differences in brain proteins between the two lines of mice (Goldman and Crabbe in press) may be related to their differing susceptibility to withdrawal seizures.

### Structural and Functional Brain Damage in Rodents

Animal, especially rodent, studies have played a vital role in attempting to approximate the probable effects of chronic alcohol consumption on the human CNS. Some alcoholics have poor dietary habits in general, and it has

been difficult to separate the effects of malnutrition in humans from alcohol's direct neurotoxic effects. Thus, animals fed nutritionally controlled diets containing alcohol have been a primary model used to isolate the effects of alcohol consumption on structural and associated functional brain changes.

Experimental evidence of alcohol's direct neurotoxicity has come from behavioral, microscopic (neurohistological), and electrophysiological animal studies conducted primarily by Walker and Hunter and their colleagues (Riley 1977; Riley and Walker 1978; Walker et al. 1980, 1981, 1982; Abraham et al. 1981, 1982, 1984). Collectively, their findings indicate strongly that alcohol administered chronically to rodents receiving a nutritionally adequate diet produces regionally specific toxic effects in the brain. The usual length of alcohol treatment required to cause these changes was 4 to 5 months. Alcohol-induced brain damage was not prevented by supplementing the diet with large quantities of vitamins and minerals.

Chronic alcohol administration produced a deterioration in the acquisition of various learning tasks. When brain tissue was examined, significant changes were found in the rodent hippocampus, including neuronal loss, alterations in the fibrous receivers (dendrites) of surviving cells, reorganization of the junctions between neurons that allow impulses to pass (synapses), and disruption of neuronal transmission. Other investigators have confirmed these alcohol-induced hippocampal changes and also have revealed alcohol effects on rodent brain mammillary bodies (Goldstein et al. 1983; Lescaudron and Verna 1985), cerebellar cortex (Tavares and Paula-Barbosa 1982; Goldstein et al. 1983; Tavares et al. 1985), and cerebral cortex and brain stem (Goldstein et al. 1983). West et al. (1982) found that in the rat dentate gyrus, heavy alcohol consumption significantly inhibits the sprouting of long fibers (axons) that transmit signals from the cell body to other cells via a synapse. Figure 6 depicts mouse cerebellar Purkinje cells before and after chronic alcohol treatment.

All these findings lend support to the view that chronic alcohol ingestion leads to cell alterations and loss in the CNS that probably are related to the functional impairment manifested by chronic alcoholics.

### Structural and Functional Brain Damage in Humans

A variety of techniques are being used to determine structural or functional organic brain deficits in humans. Because their methodological bases and capabilities differ, each technique is considered separately in the sections that follow.

#### *Autopsy Studies*

Decreased brain size (cerebral or cortical atrophy) has been a major finding in studies of alcoholic patients. It has been demonstrated repeatedly by autopsy examination and computerized axial tomography (CT scan) (Porjesz and Begleiter 1983).



Autopsy examination has revealed widespread atrophy and cell loss in many brain regions, including at least two areas of the diencephalon: (1) the mammillary bodies of the hypothalamus (Talland 1965; Angelergues 1969; Brion 1969) and (2) the middle and frontal areas of the thalamus (Porjesz and Begleiter 1983). Damage to these diencephalic structures has been reported in various memory disorders, including Wernicke-Korsakoff syndrome (Butters and Cermak 1980), an aggregate of signs and symptoms consisting of an acute (Wernicke) and chronic (Korsakoff) stage.

A recent autopsy study found brain atrophy in a significant proportion of deceased chronic alcoholic patients. Harper and Kril (1985) measured intracranial volume and brain volume (see figure 7) and calculated the pericerebral space (PICS) (see figure 8), which increases with cerebral atrophy (Harper et al. 1984). They found a significant loss of brain tissue, particularly in alcoholics with associated liver disease or vitamin B<sub>1</sub> (thiamine) deficiency (Wernicke's encephalopathy).

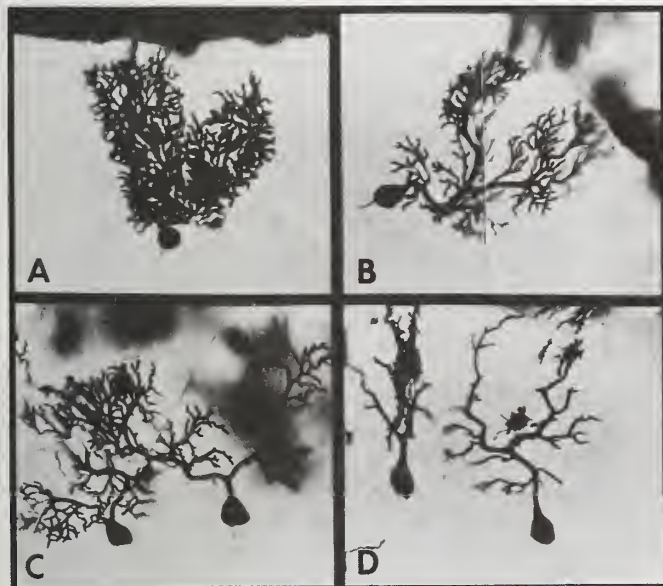
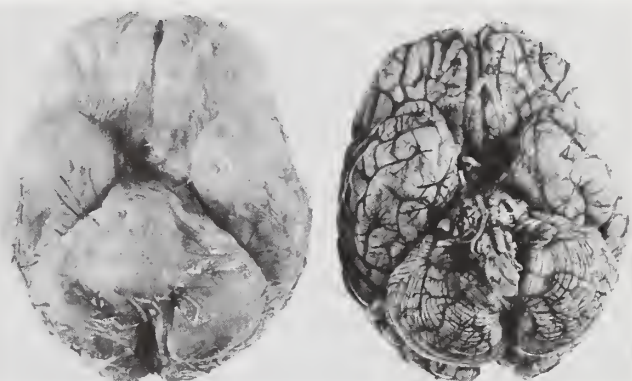


FIGURE 6. Mouse cerebellar Purkinje cells before and after chronic alcohol treatment. This photograph compares cerebellar Purkinje cells from (A) an age-matched control mouse pair-fed to an alcohol-consuming partner and (B-D) from three different alcohol-consuming mice maintained on an alcohol-containing diet for 4 months followed by 2 months without alcohol before being sacrificed. The control mice were pair-fed the same diet without alcohol and received the same daily caloric and nutrient intake. The Purkinje cells in B-D indicate severe loss of dendritic branches and virtually complete loss of dendritic spines.

Provided by Dr. Don Walker.



CAST

BRAIN

FIGURE 7. Measurement of intracranial volume and brain volume. The polyurethane foam cast (left) gives an accurate replication of the intracranial vault and allows the intracranial volume to be calculated and compared with the brain (right) volume.

SOURCE: Harper and Kril 1985.

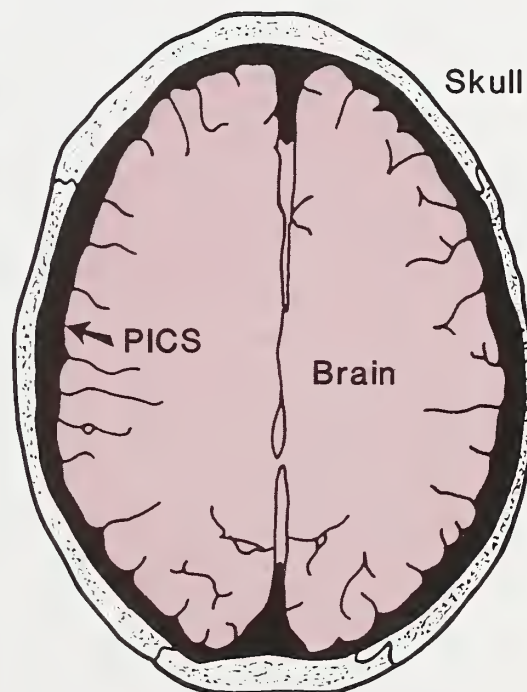


FIGURE 8. Schematic representation of the pericerebral space (PICS). It is calculated according to the equation:

$$\text{PICS} = \frac{\text{Intracranial volume} - \text{fresh brain volume} \times 100\%}{\text{Intracranial volume}}$$

and represents the "space" between the skull and the brain.

SOURCE: Harper and Kril 1985.



## CT Scan Studies

CT scan studies have provided data on structural brain abnormalities in alcoholics, but the ability of this noninvasive imaging technique to distinguish different subtypes of alcohol-induced organic brain syndrome is limited. Alcoholic dementia and alcoholic amnesic disorder (alcoholic Korsakoff's syndrome or psychosis), two clinically distinct manifestations of alcohol-induced organic brain syndrome, are believed to differ neuropathologically in the relative involvement of cortical and subcortical areas. However, it is difficult to infer the respective degree of involvement from CT scanning, because the scanning provides much less reliable quantitative information about subcortical areas than about cortical areas (Johnson et al. 1986).

Since the early 1980s, limited research on the alcoholic brain has been based exclusively on CT scans (Wilkinson 1985). CT scans often have been performed in combination with neuropsychological tests to examine the relationship between structural brain damage and intellectual impairment in chronic alcoholics. Ron (1983) studied radiologic, clinical, and psychometric data for a group of chronic alcoholics without overt clinical evidence of brain damage. Compared with controls, alcoholics had larger brain ventricles (cavities), wider cerebral sulci (grooves on the brain's surface), and wider Sylvian fissures (the largest of the cerebral furrows), and interhemispheric fissures. Cerebellar sulci were apparent only in alcoholics. When the alcoholic group was considered as a whole, some unexpected correlations were found between CT scan and psychological test results. Increasing size of the ventricular system was accompanied by good performance on tests of immediate recall and partial cued recall for figures and by poor performance on cued recall for words. Good performance on immediate recall was accompanied by increased widening of the Sylvian fissure. Gebhardt et al. (1984) found significant correlations between CT scan measures of the third ventricle region, including the dorsomedial thalamic region, and scores on tests requiring subjects to learn lists of meaningless symbols or unrelated words paired with single digits (paired-associate learning tasks). They conclude that the midline thalamic region is involved in the mediation of long-term memory.

Cala et al. (1983) analyzed the frequency of CT scan and psychometric abnormalities in a group of 39 drinkers who consumed less than 5 ounces of pure alcohol a day and related these frequencies to alcohol consumption and diet and nutritional status. Thirty-one subjects showed some degree of cerebral atrophy on CT scan, and 25 of them also performed poorly on psychometric tests. Fifteen of 16 nutritionally deficient subjects had abnormal CT or psychometric test results, but there was a lack of correlation between nutritional indexes and the presence and severity of CT scan or psychometric abnormalities. The findings suggest that these abnormalities are probably due to alcohol effects themselves rather than to associated nutritional deficiencies.

There is evidence from recent studies that some alcohol-induced brain damage and neurological impairments can

be at least partly reversed by abstinence. These studies are discussed in a later section of this chapter.

## Electrophysiology

Neuropsychological tests evaluate cognitive deficits in chronic alcoholics based on their behavior, but behavioral dysfunction may be unrelated to alcohol abuse. Similarly, CT scans give a static picture of overall structural brain damage, but they do not reveal underlying changes in brain function. Among the various methods of assessing brain dysfunction in alcoholics, Porjesz and Begleiter (1983) ascribe a unique role to evoked potential (EP) or event-related potential (ERP) noninvasive techniques. Electrophysiological brain activity can be recorded with or without accompanying behavior, and EP techniques reflect subtle functional changes that are not necessarily associated with gross brain damage.

Short-term and long-term abstinent alcoholics manifest markedly different EP patterns. CNS hyperexcitability, reflected in accelerated appearance (decreased latencies) of brain stem auditory evoked responses (BAERs) and increased EP amplitudes, may be evident up to 3 weeks following alcohol withdrawal. In contrast, alcoholics abstinent for longer than 3 weeks show CNS hypoexcitability (increased BAER latencies and decreased EP amplitudes). To distinguish the effects relating to CNS hyperexcitability from those relating to long-term brain damage (or dysfunction) and recovery, it is recommended that abstinent alcoholics be evaluated on neuropsychological performance at least 3 weeks, and optimally longer, after withdrawal (Porjesz and Begleiter 1983).

Research on electrophysiological deficits in subjects at high risk for alcoholism has produced intriguing evidence that some deficits previously thought to be *effects* of alcoholism really may be *genetic predisposition markers* of alcoholism. This topic is discussed in detail in chapter II.

## New Imaging Techniques in Alcohol Research

An exciting new addition to techniques used to study brain structure and function is positron emission tomography (PET), another noninvasive imaging technique. PET studies measure the localized brain metabolism of substances such as glucose, the brain's primary energy source. The images obtained with this technique are topographically similar to CT scans, but they reflect regional rates of glucose metabolism instead of anatomical detail (Johnson et al. 1986) (see figure 9). Unlike CT scans, PET scans provide information on subcortical as well as on cortical processes. PET scans also permit the study of biochemical and metabolic processes in the living brain (Raichle 1983; Phelps and Mazziotta 1985), thereby complementing neuroanatomical or histologic measures of structure. This technique also has been used recently to study brain receptors (Wagner et al. 1983, 1984; Baron et al. 1985; Frost et al. 1985).

Johnson et al. (1986) describe the simultaneous use of a number of complementary techniques to investigate functional CNS deficits associated with alcohol-induced organic



brain syndrome. In their laboratory these investigators are evaluating the pathophysiologic data identified by PET, referring the data to brain morphologic data obtained using CT scans, and supplementing the data with measures of CNS electrical activity (electroencephalograms—EEGs) and cognition.

Magnetic resonance imaging (MRI) is another noninvasive technique that is gaining increased attention. In this technique, a series of linear magnetic field gradients are superimposed on the static magnetic field to obtain spatial information. MRI yields brain anatomical data superior to that obtained using CT scans, as well as chemical and physiological information (Chao and Foudin 1986). Using MRI, Charness et al. (1985) consistently detected atrophy of the mammillary bodies in patients with chronic Wernicke disease, confirming in live subjects what had previously been seen at autopsy.

### Alcohol Effects on Aging

Almost identical nervous and cerebrovascular changes have been observed in the brains of rats fed alcohol chronically and in the aging rat brain (Roulet et al. 1985), suggesting that chronic alcoholism may accelerate the processes associated with biological aging. However, Shelton et al. (1984) found no support for the generalized dysfunction version of the premature aging hypothesis for performance of alcoholics on neuropsychological tests.

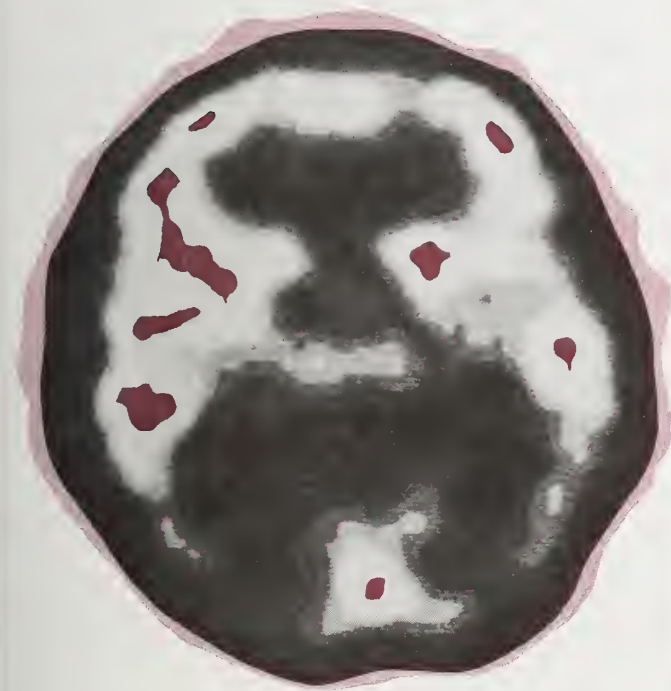


FIGURE 9. Photograph of a PET scan of a normal brain. The topographic images reflect regional rates of metabolism of glucose, the brain's main source of energy. The greatest amount of glucose is taken up in the dark red areas, and the smallest amount, in the light red areas.

SOURCE: Modified from USDHHS 1985.

Ryan and Butters (1984) propose that rather than causing premature aging, heavy alcohol intake produces diffusely distributed brain changes in humans that differ somewhat from the pattern of brain damage associated with normal aging. Thus, alcohol only mimics the alterations seen in elderly nonalcoholics. The important practical implication is that chronic alcohol abuse can cause chronic drinkers to behave *as though* they were 10 or 20 years older (Ryan and Butters 1984).

### Human Memory

Acute doses of alcohol can have a particularly disruptive effect on human memory. The BAC determines the degree of amnesia. A BAC as low as 0.04 g per 100 mL of blood disrupts memory functions, and impairment progresses as the BAC rises (Parker 1984).

Memory has been hypothesized to involve three main functions: (1) the formation of the representation of an event (encoding), (2) the translation of encodings into a lasting form (consolidation), and (3) the reawakening of the representation under particular conditions (retrieval) (Parker 1984). Experiments on amnesia after acute alcohol consumption indicate that alcohol has its primary amnesic effect on encoding activities and not on consolidation or retrieval (Parker and Weingartner 1984). Alcohol, if it is administered after an event has been encoded, facilitates memory consolidation (Esposito et al. 1984). Even though initial encoding and retrieval occur in a nondrug state, consolidation is enhanced when alcohol is ingested right after an event representation has been formed at the conceptual level. A relatively new area of research is the nature of memories susceptible to the amnesic effects of alcohol. It appears that alcohol can interfere with the ability to remember events that are encoded and consolidated, but it leaves other memory systems intact (Hashtroudi et al. 1984; Parker 1984).

### *Memory Disorders in Alcoholic Wernicke-Korsakoff Syndrome*

The Wernicke-Korsakoff syndrome is a CNS disorder resulting from the combination of severe nutritional deficiency, specifically of thiamine (vitamin B<sub>1</sub>), and protracted alcoholism. It is essentially two diseases—Wernicke's disease, a severe central nervous system disorder brought on by the thiamine deficiency—and Korsakoff's psychosis—a permanent brain disorder characterized by marked abnormalities in cognitive function, particularly the inability to remember recent events and the inability to learn new material. Although severe alcoholics may have both diseases, i.e., the Wernicke-Korsakoff syndrome, it is not clear if all Korsakoff patients have passed through a Wernicke phase. Dietary supplementation with thiamine can abate the Wernicke phase, leaving the patient with Korsakoff's psychosis with its associated memory deficits and a tendency of the patient to confabulate, i.e., to fill in memory gaps by fabricating information.

Anterograde memory deficits are a striking feature of alcoholic Korsakoff patients. This inability to acquire new

information since the onset of illness is due to increased sensitivity to interference from previously learned material (proactive interference) (Butters 1985; Butters and Brandt 1985). This memory impairment is comparable to the accelerated memory loss and increased vulnerability to proactive interference seen in mice tested on spontaneous alternation (the innate tendency of some mammals to alternate free choices in a T-maze on successive trials) following chronic alcohol treatment (Beracochea and Jaffard 1985).

Motivational and affective factors appear to play only a minor role in explaining anterograde amnesia. In one study a sexual theme facilitated Korsakoff patients' selective attention to and immediate recall of short stories better than a neutral or aggressive theme did (see figure 10), but the sexual theme had little if any influence on patients' inability to retain verbal information (rate of forgetting) (Davidoff et al. 1984). Thus, gains in selective attention do not necessarily prevent material from being forgotten quickly. The recall performance of non-Korsakoff alcoholics, however, was unaffected by the stories' emotional theme.

Alcoholic Korsakoff patients also experience severe retrograde memory deficits. Retrograde amnesia refers to difficulty in retrieving from long-term memory events that occurred before the onset of illness. This disorder may have two distinct causes: (1) the influence of chronic alcohol abuse on anterograde memory processes and (2) an acute forgetting of old memories that begins during the Wernicke phase of the illness and has an equal effect on all premorbid (prior to disease) periods. Accordingly, memory for recent events should be impaired the most, because

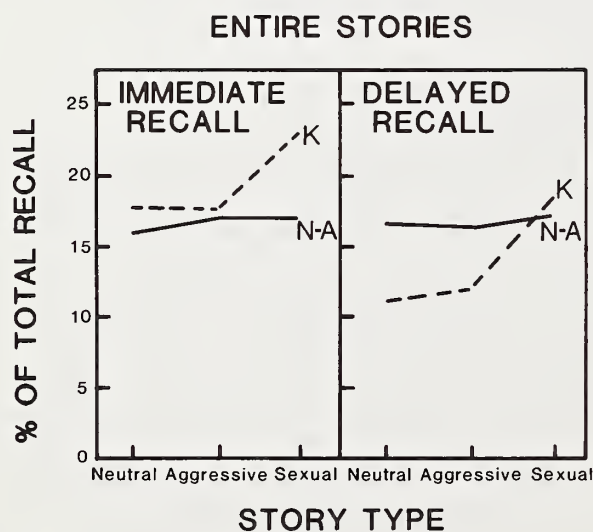


FIGURE 10. Mean percentage of total recall for the combined normal control and long-term alcoholic (N-A) and alcoholic Korsakoff (K) groups. Scores are shown for immediate and delayed recall for the three types of short stories.

SOURCE: Davidoff et al. 1984.

recently acquired information is less stable than material stored earlier (Butters 1985; Butters and Brandt 1985). A case study of a renowned scientist and university professor who developed alcoholic Korsakoff's syndrome at age 65 provides strong support of this two-factor model of Korsakoff patients' retrograde memory impairment. As seen in figure 11, the subject demonstrated severe retrograde amnesia for persons he once knew well, with relatively greater impairment shown for the most recent decades (Butters and Cermak 1983; Butters 1984). Thus, this form of amnesia cannot be attributed to a progressive learning deficiency alone.

It appears that anterograde and retrograde amnesia can be dissociated from one another and may involve different CNS circuits (Butters 1985; Butters and Brandt 1985). The exact neural circuits underlying anterograde and retrograde memory processes are unknown, but a report based on stimulation studies in epileptic patients revealed evidence for such an anatomic separation within the temporal lobes (Fedio and Van Buren 1974).

### *Etiology of Alcoholic Korsakoff's Syndrome*

Evidence from autopsy (Victor et al. 1971) and CT scan studies (Wilkinson and Carlen 1981) links alcoholic Korsakoff's syndrome to the middle area of the diencephalon (especially the dorsomedial nucleus of the thalamus). However, on the basis of a demonstration of similarities in the memory disorders of Korsakoff and Alzheimer patients, Arendt et al. (1983) propose that Korsakoff's syndrome is a basal forebrain, rather than diencephalic, amnesia. They suggest that the critical area affected in alcoholic Korsakoff patients may be a mass of nerve cells in the forebrain that send signals to the hippocampus and cerebral cortex. This structure is called the nucleus basalis of Meynert (NbM). Acute thiamine deficiency combined with heavy alcohol use may cause cell death within this structure, thereby decreasing neurotransmission to the brain areas that control memory functions.

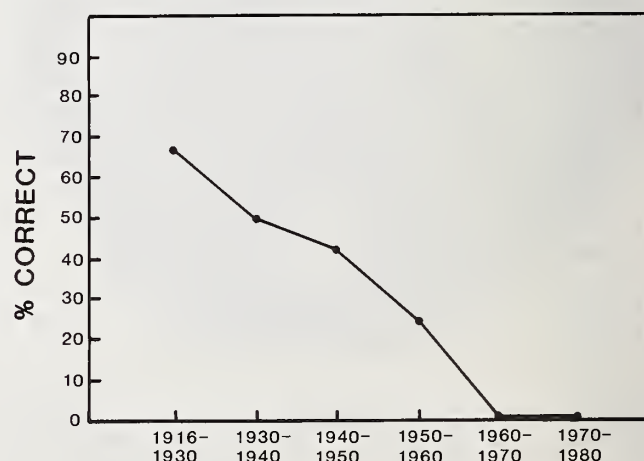


FIGURE 11. Patient's retrograde amnesia for information from his published autobiography.

SOURCE: Butters 1984.



The proposed association between thiamine deficiency and the NbM rather than the medial diencephalon is supported indirectly by animal studies on the neuropathological effects of insufficient vitamin B<sub>1</sub> (Butters 1985). Neither Irle and Markowitsch's study (1983) of thiamine deficiency in rats nor Witt and Goldman-Rakic's studies (1983a, b) of thiamine deficiency in monkeys revealed lesions of the diencephalon.

Although avitaminosis has been widely regarded as the primary cause of Wernicke-Korsakoff syndrome, there is now impressive evidence that chronic alcohol consumption unaccompanied by malnutrition results in permanent learning deficits and significant brain damage in rodents. Further research is needed to shed more light on the complex etiology of this syndrome and to determine whether it is essentially a basal forebrain or diencephalic amnesia (Butters 1985).

### Social Drinking

Alcoholics are not the only people at risk for sober cognitive deficits. The phrases "social drinking" and "social drinker" are used routinely in studies of the effect of alcohol on the normal brain. The critical issues are really the quantity of alcohol consumed per occasion (QPO) and the time period during which alcohol is consumed. "Social drinker" can refer to someone who drinks a glass of wine or two at social functions just as it can describe a person who consumes large amounts of alcohol without clinical repercussions (Parker 1984, 1985). These are vague terms, and their meanings vary in different cultures. College students—frequent subjects in studies of nonalcoholic drinkers—often are identified with social drinkers, despite the fact that a significant number of them are heavy drinkers (Hannon et al. 1985).

Investigations of sober cognitive function in nonalcoholic subjects have yielded disparate results. The studies show ambiguous or inconsistent findings (Parsons and Fabian 1982; Hannon et al. 1983), no correlation between QPO and neuropsychological performance (Bergman et al. 1983), a partial correlation (MacVane et al. 1982), or mild cognitive deficits in male heavy drinkers (Bergman 1985) or female heavy drinkers (Parker et al. 1983). Decrements in cognitive performance may be greater in older than in younger nonalcoholic drinkers (Noble 1983).

Some investigators have found CT evidence of early effects of alcohol on the brain (Cala et al. 1978; Cala 1985), whereas others have not (Bergman et al. 1983). There seems to be no direct correlation between CT findings and alcohol consumption pattern. Rather than indicating measurable brain atrophy, the reduced cognitive function that has been found may reflect a transient hangover effect from alcohol or its metabolites, an effect that may be expressed as subtle cognitive loss (Parker 1984; Hill and Ryan 1985).

For the present, then, the theory that moderate alcohol consumption will cause permanent, structural brain damage remains unsubstantiated. Nonetheless, the cognitive

efficiency of even moderate social drinkers may be compromised (Jones and Jones 1980; Parker et al. 1980; MacVane et al. 1982; Parker et al. 1982; Parsons and Fabian 1982; see also review by Noble 1983).

### Reversibility of Brain Damage and Neuropsychological Impairment

Recent evidence suggests that alcohol-induced damage to dendrites in the rat hippocampus may be at least partially reversible with abstinence (McMullen et al. 1984; King et al. 1985). Long-term potentiation—a form of synaptic flexibility (plasticity) lacking in memory-deficient aged rats (Landfield and Lynch 1977)—has been found to be depressed in the hippocampus of rats fed alcohol chronically, but this depression was partially reversible in some cases when alcohol was withheld (Durand and Carlen 1984). These findings await further confirmation and possible application to humans.

Reversibility of alcohol's neurotoxic effects may account for some disparate human and animal findings. Not all the alterations in the number or affinity of neuronal receptors for neurotransmitters or neuromodulators reported in animal brains (Tabakoff and Hoffman 1983) have been found in the brains of alcoholics. Few changes have been observed in receptors or enzymes in human brains, but the changes that do occur seem to parallel animal findings. Other disease processes occurring concomitantly with alcohol abuse in humans may produce biochemical changes opposite to those produced by alcohol, thereby masking alcohol's effects. It is also possible that biochemical brain changes seen in animals treated chronically with alcohol are less evident in humans or are reversible when drinking ceases (Tabakoff et al. 1985).

Studies of the long-term reversibility of brain changes observed on CT scans often produce dissimilar results, so this issue remains essentially unresolved. Carlen et al. (1984) studied recently abstinent alcoholics with repeated neuropsychological tests and repeated CT scans. Significant improvement of cognitive deficits and partial reversibility of brain atrophy began to be observed soon after drinking stopped (see figure 12). However, the results may have reflected recovery from the alcohol withdrawal syndrome. Ron (1983) found a tendency toward normalization of the width of the sulci and Sylvian fissures in alcoholics who remained abstinent for a period of 30 to 152 weeks or had only brief relapses, but their cognitive performance did not differ significantly from that of patients with unchanged drinking patterns. However, Cala et al. (1983) observed reversal of cerebral atrophy in 10 of 11 subjects who abstained from alcohol for 3 to 12 months, and 5 of the subjects showed improved memory performance and overall intellectual function. The reason for the disparity of these findings is unknown, but it may be partly due to different methods for measuring cognitive functions. Further investigation is needed in this area.

The problem of residual withdrawal symptoms complicates the few reported attempts to assess the reversibility of

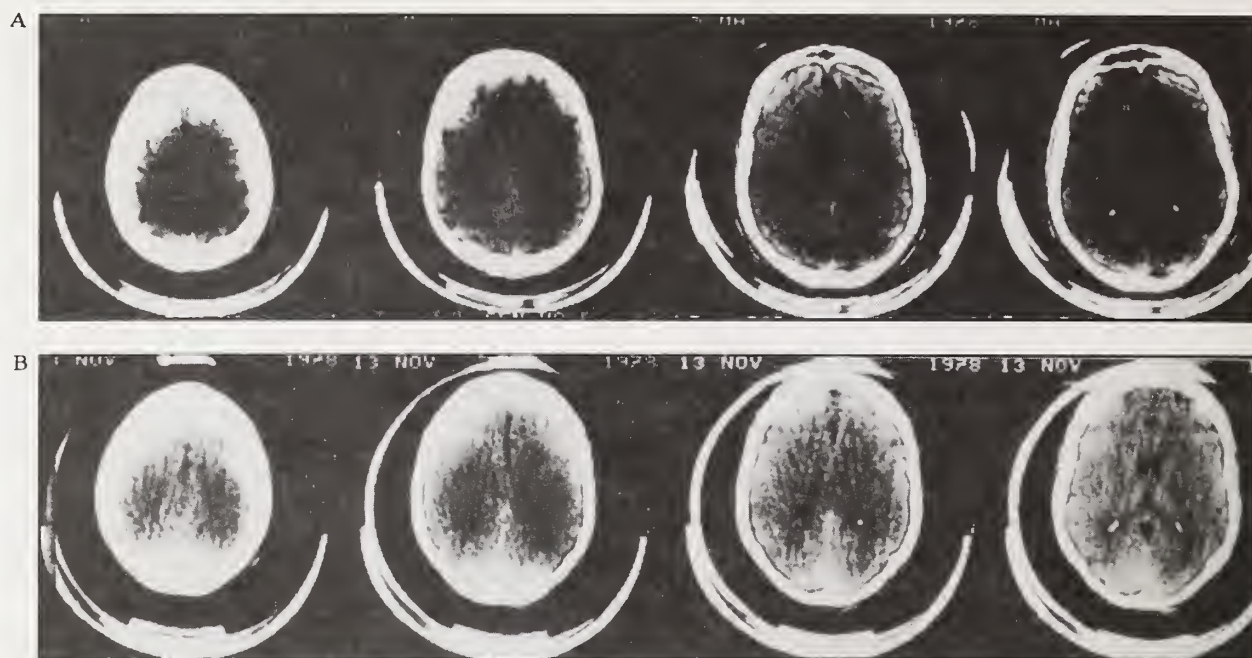


FIGURE 12. Repeated CT scans of a recently abstinent 32-year-old male alcoholic. These were done 10 days (A, upper panel) and 115 days (B, lower panel) after the day of his last drink. He was reportedly abstinent during the interscan interval. Note considerably decreased cerebral cortical sulcal and ventricular atrophy in the second scan.

SOURCE: Carlen et al. 1984.

electrophysiological brain deficits. What seems to be recovery may really represent the reversibility of physiological changes accompanying withdrawal (e.g., fluid accumulation in brain tissue) or recovery from other forms of brain damage. Porjesz and Begleiter (1985) have been examining the BAERs and ERPs after 3 weeks and 3 to 4 months of continued abstinence in hospitalized alcoholics. The preliminary brain stem potential (BSP) findings after almost 4 months of abstinence in one alcoholic (see figure 13) indicated improved wave form morphology, reduction of latencies, and improved conduction times. Data for the group as a whole, however, indicate that the wave form peaks still occur somewhat later in alcoholics than in controls.

Partial support for the view that alcohol-induced brain deficits may be more reversible in younger subjects is provided by Goldman et al. (1983), who found a better prognosis for recovery of visuospatial capacity within several weeks of cessation of drinking in younger alcoholics (under age 40) than in older alcoholics. Learning and memory impairment persisted in both age groups, however. Brandt et al. (1983) assessed the degree of deficit and the effects of abstinence over a 5- to 10-year period. They observed that young men, even those with extended sobriety, were as vulnerable to alcohol's damaging effects as older men. Memory and visuospatial defects associated with chronic alcoholism were investigated in male subjects who had been abstinent for at least 5 years. Short-term memory and psychomotor skills improved significantly with prolonged abstinence, but long-term memory and the ability to learn novel associations were impaired at all ages

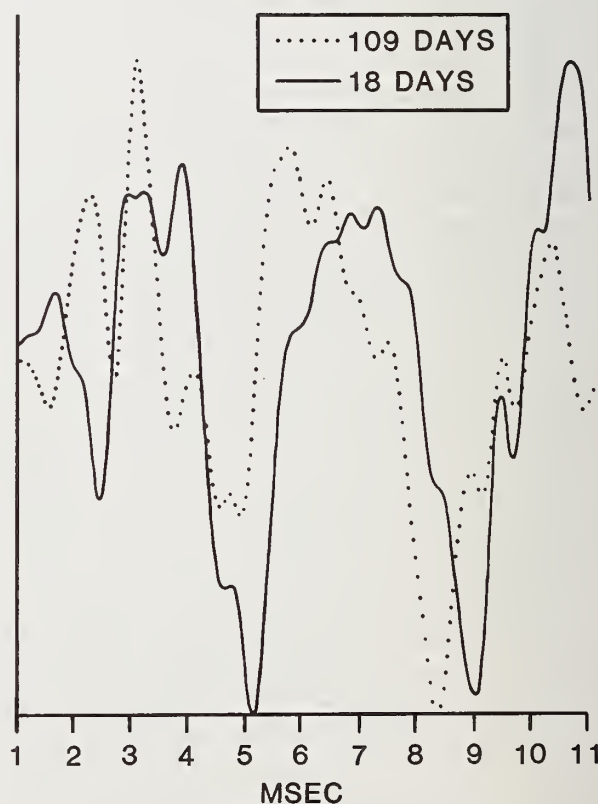


FIGURE 13. Auditory brain stem potential (BSP) in a chronic alcoholic after 18 days (solid line) and 109 days (dashed line) of abstinence. Notice that the latency of the major large complex (waves IV to V) occurs earlier after prolonged abstinence.

SOURCE: Porjesz and Begleiter 1985.



even after 7 years of sobriety. The investigators propose that recovery of short-term memory reflects reestablishment of cortical functioning, whereas the persistent impairment of long-term memory suggests more permanent damage to limbic-diencephalic structures (e.g., the hippocampus, dorsomedial nucleus of the thalamus, and mammillary bodies).

Yohman et al. (1985) evaluated detoxified male alcoholics with some similar results. Alcoholics had protracted deficits in cognitive and perceptuomotor skills relative to nonalcoholics even 13 months from the start of detoxification. An unexpected finding was the damaging effect on verbal skills, previously thought to be resistant to alcohol. This was a very mild but statistically significant deficit. Lack of improvement in the alcoholic group's performance was due in part to the resumption of drinking, even at a reduced level, by some alcoholics, usually those with the greatest cognitive impairment. Analogous results have been obtained with recovering alcoholic women (Fabian and Parsons 1983).

## SUMMARY

Alcohol can have profound effects on both the structure and function of the central nervous system. The effects are expressed first at the level of the neuronal membrane, where they are quite selective. Alcohol's membrane-disordering effect can be small, but this effect ultimately can involve a neuron's ability to conduct and transmit information, a process crucial to brain function. Alcohol has multiple sites of action, and different neurotransmitter systems have differing sensitivity to alcohol's actions.

Chronic consumption of alcohol appears to result in an adaptation within the neuronal membrane that is manifested as alcohol tolerance, physical dependence, and alcohol withdrawal syndrome. Alcohol tolerance and physical dependence are distinct effects of alcohol ingestion, but they are closely linked in that the presence of tolerance in a person can necessitate or permit the consumption of alcohol in amounts that can lead to physical dependence.

As alcohol's effects on the brain neuronal membrane are selective, so is alcohol-induced structural brain damage regionally specific. One of the principal aims of alcohol-related research on the brain is to correlate neurochemical and anatomic changes with behavioral and physiological responses to alcohol. The use of PET and other new noninvasive imaging techniques promises to advance research on functional CNS deficits associated with alcohol-induced brain damage.

An exciting byproduct of research on alcohol-induced electrophysiological deficits in alcoholics has been the finding that some deficits previously thought to be effects of alcoholism actually may be antecedent and biological markers of the disease (see chapter II).

Recent studies on memory suggest that alcohol can interfere with the memory system that enables people to be aware of information that is encoded and consolidated during alcohol intoxication. Research on the etiology of

alcoholic Korsakoff's syndrome, a severe amnesic disorder, is focusing on etiology. At present it is debatable whether this disorder is essentially a basal forebrain or diencephalic amnesia.

Alcoholics are not the only people at risk for cognitive deficits. There is still controversy as to whether moderate alcohol consumption will cause permanent structural brain damage, but it is clear that the cognitive efficiency of moderate social drinkers can be compromised.

The reversibility of alcohol-induced organic brain damage and neuropsychological impairment remains one of the most controversial yet important issues in all of alcohol-related research. Recovery from the alcohol withdrawal syndrome and the existence of residual withdrawal symptoms often complicate the interpretation of findings in studies on long-term reversibility of functional brain changes.

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# Medical Consequences of Alcohol

**D**irectly or indirectly, alcohol affects virtually every organ system in the body: digestive, nervous, endocrine, reproductive, musculoskeletal, cardiovascular, immune, and respiratory. This chapter describes some of the diverse and complex effects of alcohol on the body, with emphasis on the most recent research concerning the mechanisms by which these effects are caused.

## EFFECTS ON THE DIGESTIVE SYSTEM

### The Stomach

When alcohol enters the stomach, it can alter the stomach mucosa (lining) and affect gastric functioning. In vitro animal studies have shown that alcohol at a concentration of 8 percent or less can stimulate gastric acid secretion (Davenport 1967). In other animal studies, stronger solutions have been seen to inhibit acid secretion (Tuyns 1979). Wine has been reported to be a strong stimulant of gastric acid secretion in humans, whereas beer and diluted whiskey are weak stimulants (Lenz et al. 1983).

Recent studies have demonstrated profound changes in gastric mucosa in rats 10 minutes after administration of 2 mL of absolute alcohol (Tarnawski et al. 1983). Over time, hemorrhagic lesions spread over a large mucosal area, and after an hour injury was evident in 20 to 33 percent of the gastric mucosa in the rats. Light microscopy revealed extensive lesions penetrating deeply into the mucosa, along with a desquamation (shedding) of the mucosal epithelium (surface cell layer). Scanning electron microscopy revealed large craters in the connective tissue layer. Although desquamation was extensive at first, it was no longer detectable after 6 hours. In humans, this pathology would be called acute gastritis (Palmer 1954).

Although most studies do not implicate alcohol as a cause of gastric ulcers (see review by Kurata and Haile 1984), there are reports that alcohol, when taken with aspirin or other substances known to irritate the stomach, can cause marked gastritis, gastric ulcers, and sometimes severe bleeding (Tariq et al. 1986; see also review by Mendelson and Mello 1985), and it has been confirmed that alcoholics have a greater tendency to develop chronic gastritis than nonalcoholics do (Parl et al. 1979). Other research, however, suggests that a tolerance to mucosal injury develops with chronic alcohol exposure (Ivey et al. 1980).

Until recently, it was believed that practically all alcohol was absorbed intact from the gastrointestinal tract and was metabolized mostly in the liver (Lieber 1982b). Julkunen et al. (1985) recently found that much of the alcohol that is consumed in small doses is metabolized in the stomach. It is hypothesized that this gastric metabolism acts as a barrier to toxicity with moderate alcohol doses, but that chronic alcohol consumption diminishes the barrier's effectiveness because of depletion of gastric alcohol dehydrogenase.



## The Intestine

The direct effects of alcohol on the small intestine can include changes in intestinal motility, metabolism, blood circulation, and cellular structure (Lieber et al. 1982). High concentrations of alcohol directly affect epithelial cell function and survival (Lieber et al. 1982). In hamsters, exposure of the jejunum (a segment of the small intestine) to physiologic levels of alcohol can result in fluid-filled blisters and vascular engorgement of the intestinal villi, which are short filament-like processes found on the intestinal membrane surface (Fox et al. 1979). Similar blisters were seen in biopsies from human volunteers after intragastric instillation of an amount of alcohol equivalent to 5 ounces of 80-proof whiskey (Millan et al. 1980).

People for whom alcohol constitutes a significant portion of their caloric intake often do not eat enough food to ensure a supply of essential nutrients. As a result they may suffer not only primary malnutrition resulting from an inadequate diet, but also secondary malnutrition from the effects of alcohol on nutrient digestion, absorption, or subsequent use by the body (see figure 1). Thiamine (Hoyumpa 1983), folic acid, and other vitamin deficiencies as well as disorders resulting from amino acid imbalances may be seen in alcoholics (Lieber 1984b). Diarrhea and malabsorption, which are common in heavy drinkers and alcoholics, result from direct toxicity of alcohol on the intestine as well as from a variety of other interacting factors, such as malnutrition and injury to the liver and pancreas.

Measurements of albumin excretion suggest that a loss of protein due to intestinal dysfunction may contribute to malnutrition in chronic alcoholic patients (Bretagne et al. 1982). However, other investigators (Bjarnason et al. 1984) who have examined intestinal mucosal permeability in

nonintoxicated alcoholic patients who were not cirrhotic have found no evidence of malabsorption or malnutrition. Patients who abstained from alcohol for less than 4 days almost always had higher mucosal permeability in the small intestine than controls did. In many patients this increased permeability persisted up to 2 weeks after drinking was stopped. The clinical significance of the changed permeability is not clear; no clinical symptoms could be specifically related to it. However, it has been suggested that increased intestinal permeability could result in absorption of toxic compounds that are otherwise not absorbable, and that this could accelerate damage commonly seen in alcoholics in parts of the body other than the intestine (Bjarnason et al. 1984).

Injury to the intestinal tract may also take the form of varices (twisted and dilated veins or arteries) in the colon, which, though rare, may cause sudden massive rectal bleeding in patients with liver cirrhosis (Lieber et al. 1982). Alcohol may also have direct effects on colonic motility and morphology. As described in a later section, an increased incidence of colon cancer has also been reported in alcoholics.

## Effects on the Liver

It is well established that the liver is the primary site of alcohol metabolism; that alcohol abuse can cause changes to the liver in the form of fatty liver, alcoholic hepatitis, or cirrhosis; and that these changes can occur even when there is no malnutrition (Lieber and DeCarli 1970). In the United States, alcohol abuse is the leading cause of cirrhosis, which is itself the ninth leading cause of death (Grant et al. 1986). In at least one urban area, New York City, alcoholic cirrhosis was the third leading cause of death in 1979 among persons 25 to 65 years old (Lieber and Leo 1982).

Most evidence indicates that alcoholics who develop cirrhosis consume large amounts of alcohol. In one survey (Lelbach 1975), the mean consumption was 160 grams—the equivalent of approximately 13 drinks a day for an average of 20 years, whether the drinks were 12-ounce glasses of beer, 5-ounce glasses of wine, or mixed drinks. However, far lower intake has been implicated in an increased risk for developing cirrhosis. A French study indicates that as little as 40 grams (three drinks) for men and 20 grams (one and one-half drinks) a day for women may increase the risk of developing the disease (Pequignot and Tuyns 1980).

Not all heavy drinkers will develop these complications of alcohol abuse, however, and the amount of alcohol consumed is not an accurate indicator of those who may develop the disease. For persons who do develop cirrhosis, it is an irreversible condition with an average 50 percent survival rate after 5 years (Mezey 1982).

The pathology of alcoholic liver disease includes hepatic steatosis (fatty liver), hepatic fibrosis (formation of scar tissue in the liver), alcoholic hepatitis (inflamed liver), and cirrhosis (Lieber 1982b). Fat accumulation in the liver, the earliest and most common effect of alcohol consumption, is generally considered benign and reversible, and there is no evidence that the condition is a precursor to cirrhosis.

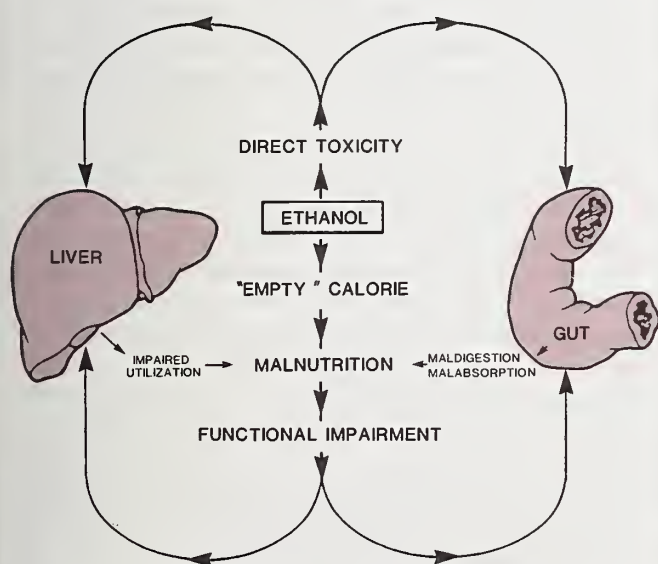


FIGURE 1. Interaction of direct toxicity of ethanol on liver and gut with malnutrition secondary to dietary deficiencies, maldigestion, and malabsorption.

SOURCE: Lieber 1982a.



Alcoholic hepatitis is characterized by an inflammatory reaction and death of liver cells. Although the prognosis for alcoholic hepatitis is approximately 60 percent survival 5 years after the onset of the disease, as many as 49 percent of patients with severe disease, if untreated, may die within a few months (Alexander et al. 1971).

The mechanism for the development of cirrhosis has commonly been described as a response to alcoholic hepatitis; it has been thought that the inflammation and necrosis trigger the scarring process of cirrhosis (Lieber 1982b). However, more recent studies indicate that cirrhosis may develop without an intermediate stage of alcoholic hepatitis (Karasawa et al. 1980; Nakano and Lieber 1982; Takada et al. 1982). In the studies of Nakano and Lieber (1982), 20 alcoholics had sequential liver biopsies as part of their medical evaluation. Of 10 patients with simple fatty liver, 9 showed no histological liver changes after 1 to 2 years, even though they continued to drink. However, among 10 patients with a condition called perivenular fibrosis, which is characterized by scarring around the central or terminal veins or venules of the liver, all who continued to drink did show progression, some to cirrhosis, without evidence of passing through an intermediate stage of hepatitis.

Work by Worner and Lieber (1985) has provided further detailed observations on perivenular fibrosis as a precursor of cirrhosis. Thirty-four male alcoholics underwent sequential liver biopsies. Of 19 patients with simple fatty liver, only 3 showed progression of liver disease. By contrast, of 15 subjects with perivenular fibrosis at the time of the initial biopsy, 13 progressed to more severe stages of liver disease during a 1- to 4-year followup. This finding suggests that the presence of perivenular fibrosis may mark the beginning of a process that leads to cirrhosis. Because of its prognostic value, early detection of perivenular fibrosis may be of value in the care of alcoholic patients, but obtaining the required liver biopsies would not be practical for large-scale disease identification or control (Lieber 1982b).

Studies by Lieber et al. (1981) and Nakano and Lieber (1982) have reported the occurrence of myofibroblasts (cells from which connective tissue develops) in nonfibrotic, nonscarred human liver and in livers of normal control animals. These same studies also indicate that an increase in these cells is detectable very early in the fibrotic process. Because perivenular fibrosis developed in livers that showed only fatty changes, it was suggested that alcohol or its metabolites may provoke the active proliferation of myofibroblasts. Lieber et al. (1981), in fact, found that the number of myofibroblasts surrounding terminal liver venules increased after alcohol exposure even before the terminal venules thickened. The appearance and proliferation of small fibers and other structures containing collagen, a major protein component of scar tissue, correlated with the localization of the myofibroblasts, suggesting that these cells may play a key role in the fibrotic process initiated by alcohol (Lieber 1985).

The accumulation of hepatic collagen during the development of cirrhosis may be due to increased collagen synthesis, decreased collagen degradation, or a combina-

tion of the two mechanisms. In cultured myofibroblasts from baboons, both lactate and acetaldehyde (the latter being the first product of ethanol metabolism) have been found to stimulate collagen synthesis (Savolainen et al. 1983).

During collagen formation, propeptides (parts of the molecule of a collagen antecedent known as a procollagen) are released into the blood stream. Serum concentrations of the propeptide known as PRO-(III)-N-P correlate with the hepatic fibrotic activity in chronic liver disease and have been found to be increased in alcoholic hepatitis and cirrhosis (Ackerman et al. 1981). However, Lieber (1985) has suggested that, in alcoholic liver disease, serum collagen propeptide concentrations do not indicate early stages of fibrosis but appear to relate more to inflammation. The highest levels of the propeptide were found in a subgroup of patients with alcoholic hepatitis.

Collagen deposition, decreased openings in the minute blood vessels of the liver known as sinusoids, and perivenular fibrosis may increase resistance to blood flow and may play a role in portal hypertension (increased blood pressure in the portal vein, which carries blood from the intestine to the liver). Although a study by Møreland et al. (1981) found that acute ethanol administration had no influence on the rate of protein secretion by suspensions of rat hepatocytes (the predominant cells in liver), other studies have suggested that expansion of hepatocytes and reduction of extracellular space also may play important roles in portal hypertension. Biopsy studies by Vidins et al. (1985) demonstrated a reduction in liver sinusoidal areas in alcoholic liver disease that did not occur in patients with nonalcoholic liver disease or in normal controls. The observed difference between alcoholic and nonalcoholic patients was large enough to suggest that measurement of liver sinusoidal areas by biopsy might be used to differentiate alcoholic liver disease from nonalcoholic liver injury, especially chronic hepatitis. These studies support the suggestion that enlargement of hepatocytes and compression of the sinusoids may play a role in causing portal hypertension (Orrego et al. 1981; Blendis et al. 1982; Israel et al. 1982).

There is no established therapy for patients with alcoholic liver cirrhosis, and about half of such patients die within 5 years. Deficiencies in lipotropic compounds such as choline and methionine, which promote the transportation and use of fats and help prevent accumulation of fat in the liver, have produced fatty liver and cirrhosis in rats (Best et al. 1949). This suggests that administration of lipotropic compounds might prevent or reverse alcohol-caused liver injury. However, clinical treatment with added choline has been found ineffective in patients with alcoholic liver injury when alcohol abuse continues (Post et al. 1952; Phillips and Davidson 1954; Olson 1964). In fact, even massive supplementation with choline failed to prevent the development of fatty liver in volunteer subjects (Rubin and Lieber 1968). Lieber et al. (1985) found in studies with baboons that choline treatment not only failed to prevent liver fibrosis but even exerted some toxic effects. With ethanol-containing diets, with or without



choline supplement, the animals developed fatty livers, liver cell damage (mitochondrial lesions), increased serum bilirubin, and other indications of liver dysfunction.

Features of cirrhosis indicating a poor prognosis are changes in blood chemistry and blood clotting, gastrointestinal hemorrhage, brain disorders (spontaneous encephalopathy), kidney problems (hepatorenal syndrome), and accumulation of fluid in the peritoneal cavity (ascites). Increased fibrosis and continued alcohol abuse will also adversely affect the prognosis (Schenker 1984). Liver transplantation has been tried in 25 patients. Of these patients, 40 percent have survived 1 to 3 years.

Serum gamma-glutamyltranspeptidase (SGGT) has been found to be a useful index of alcohol-induced liver injury (Moussavian et al. 1985). In patients without clinically obvious liver disease, the elevations of SGGT were 2 to 3 times the upper limit of normal, but the levels fell to normal in 80 percent of patients within 8 weeks of abstinence. In contrast, in patients with liver disease the elevations of SGGT were 8 to 10 times the normal level and persisted at these high levels after 8 weeks of abstinence. Because the SGGT level did not correlate with alcohol consumption, an elevated SGGT level may be an indicator of alcohol-induced liver injury rather than of alcohol consumption as such.

Evidence that thyroid hormone or a similar factor may be involved in liver damage from alcohol is discussed in the section of this chapter on the Effects on the Endocrine and Reproductive Systems.

## EFFECTS ON THE CARDIOVASCULAR SYSTEM

Heavy alcohol consumption has been shown to increase the mortality from coronary heart disease (CHD) and the risk for cardiovascular diseases in general (Sundby 1967; Pell and D'Alonzo 1973; Wilhelmsen et al. 1973; Dyer et al. 1977; Shaper et al. 1981). Although the increased mortality and morbidity may result from the direct toxic effects of ethanol on the heart (Knott and Beard 1982), other systemic effects of alcohol may contribute to circulatory diseases. These effects include hyperlipidemia (increased concentrations of lipids in the blood), vitamin deficiencies, protein deficiency, carbohydrate intolerance, hypoglycemia (low blood sugar), abnormalities in mineral metabolism, and alterations in calcium metabolism. All of these have been shown to contribute in some degree to circulatory disease.

### The Heart

In normal subjects, alcohol decreases resistance to blood flow throughout the body, causing a reduction in blood pressure and a consequent improvement in cardiac output, even though alcohol has a direct depressant effect on the heart (Friedman et al. 1982). Two recent studies have shown that acute alcohol consumption causes functional changes in heart tissue even in young adults (Kelbaek et al. 1985; Lang et al. 1985). Lang et al. (1985) studied nine healthy young men, using echocardiography and calibrated carotid pulse tracings and found myocardial depression.

These effects appear to be dose-dependent and reduce cardiac contractility only during alcohol intoxication (Kelbaek et al. 1985). The changes appeared to be more pronounced at rest than during exercise, but the researchers suggest that compensatory mechanisms may have reduced the effects during exercise.

The effects on contractility may result from direct effects on the cardiac muscle itself. In skeletal muscle, exposure of the tissue to alcohol results in increased membrane conductance, lowered membrane resistance, and decreased resting membrane electrical potential (Knott and Beard 1982). Changes in potassium, magnesium, and calcium ion concentrations also may be involved. The results, the researchers suggest, are heightened excitability, increased conduction time, and prolonged depolarization and repolarization time. In addition, the effects of alcohol are also seen in the heart's impulse-conducting tissue, which is responsible for triggering coordinated contractions of the heart muscle fibers (Knott and Beard 1982).

Although the net effects in healthy, nonalcoholic individuals may be small, it has been suggested that, in patients with congestive cardiomyopathy, the effects will vary according to the relative influence of alcohol-induced peripheral vasodilation, myocardial depression, and the degree of underlying cardiac reserve (Segel et al. 1984). For example, alcohol may depress cardiac output in patients with fully compensated left ventricular dysfunction. However, in patients with low cardiac output, alcohol-induced changes in peripheral resistance with no concomitant change in the already depressed cardiac output may cause lower blood pressure in the aorta, the body's main artery (Friedman et al. 1982). Therefore, cardiac patients may behave in a totally atypical manner depending on their history of alcohol abuse, their particular psychophysiologic response, and the associated effects of alcohol and reduced heart function on blood pH, lactate, acetate, and acetaldehyde.

In chronic alcoholics, there is a form of cardiomyopathy that is characterized by an actual wasting of the heart muscle. In experimental animals, chronic exposure to alcohol produces disturbances in electrolytes, metabolism, and contractility (Polimeni et al. 1983), but currently there is no good animal model for the muscle wasting observed in humans. There is some evidence that alcoholic cardiomyopathy results from prolonged exposure to the toxic effects of alcohol or acetaldehyde or cardiac mitochondria (Wendt et al. 1965; Segel et al. 1979). The observed defects include mitochondrial enlargement, depressed mitochondrial respiration, liberation of mitochondrial enzymes into the blood, reduced levels of mitochondrial adenosine triphosphate (a chemical that supplies energy for numerous metabolic processes), and reduced ion transport. Some investigators have suggested that acetaldehyde directly mediates this damage (Lang et al. 1985), since acetaldehyde increases heart rate, systemic arterial pressure, and myocardial contractile forces. It also reduces cardiac microsomal protein synthesis and produces morphological and biochemical evidence of injury to the mitochondria. However, others have questioned whether acetaldehyde can accumulate in tissues such as the heart in concentrations



that are sufficient to cause disease (Taraschi and Rubin 1985).

Other research suggests that production and accumulation of fatty acid ethyl esters in heart tissue may be involved in the development of alcohol-associated cardiomyopathy. Lange and Sobel (1983) demonstrated an accumulation of these compounds, which results from an enzyme-catalyzed reaction between alcohol and free fatty acids, in heart muscle. These researchers suggest that it may be the ethyl esters rather than alcohol or acetaldehyde that are toxic. They hypothesize that these esters bind to the mitochondria and then hydrolyze to toxic fatty acids that may disrupt mitochondrial energy metabolism. Other studies (Lange and Sobel 1983; Mogelson and Lange 1984) have shown that both human and animal hearts metabolize ethanol to form these fatty acid ethyl esters.

Heart conduction disturbances can also occur in chronic alcohol users, both with and without an underlying cardiomyopathy. Arrhythmias known as the "holiday heart syndrome" have been seen in chronic alcohol drinkers, particularly after periods of heavy drinking (Greenspon and Schaal 1983). Many patients have been seen with atrial flutter and fibrillation (irregular and sometimes rapid contractions of the upper chambers of the heart), suggesting that alcohol can disrupt normal cardiac rhythms (Ettinger et al. 1978).

### The Vascular System

Associations between alcohol consumption and elevated blood pressure have been seen in several population studies (Arkwright et al. 1984). A Kaiser-Permanente study (Klatsky et al. 1977) found that the increased blood pressure associated with alcohol consumption was not affected by obesity, age, cigarette smoking, coffee or tea consumption, education, or exercise. No obvious threshold effect for alcohol consumption was apparent, but a linear relationship was found between alcohol consumption and systolic blood pressure. A cause-and-effect relationship between alcohol consumption and hypertension was suggested, as was a genetic factor that independently predisposes a person both to drinking and to hypertension.

A more recent study by Malhotra et al. (1985) found no significant difference either before or after alcohol consumption in subjects who had blood pressure in the normal range and drank amounts of alcohol equivalent to 1 g/kg body weight (equivalent to approximately five and one-half standard drinks for a 160-pound subject) daily for 5 days. However, in nondrinkers whose blood pressure was already raised, both systolic and diastolic pressures were further elevated when the subjects were drinking. In regular drinkers with already raised blood pressure, systolic and diastolic pressures were also significantly higher when subjects were drinking than when they were not.

A similar aggravation of hypertension by alcohol was reported by Potter and Beevers (1984). In this study, eight hypertensive male hospital patients who were social drinkers abstained for 3 days, then were given four beers a day for 3 days. Blood pressure, especially systolic pressure, fell during the 3 days of abstinence, but both systolic and

diastolic pressure rose significantly during the 3 days when drinking was resumed. A recent cross-sectional survey of 491 healthy young men (Arkwright et al. 1982) found that systolic blood pressure rose significantly with increasing amounts of alcohol consumed on a daily basis although the mechanisms for these effects have not been established.

Arkwright et al. (1984) have suggested that the blood pressure effects of alcohol may be associated with enhanced calcium transport and with a short-term rise in plasma adrenaline and a longer-term rise in plasma levels of the hormones noradrenaline, cortisol, and renin.

Diseases involving thromboses (blood clots that obstruct a blood vessel), including peripheral venous thrombosis, pulmonary embolism, and ischemic brain infarction (stroke), are thought to be more common in alcoholics. Hillbom et al. (1984) examined the function of platelets (blood elements involved with clotting) in withdrawing alcoholics. The platelet counts of 10 alcoholics were depressed upon admission to an inpatient detoxification program. Later, five patients showed a rebound increase in platelets, and five had normal or above-normal platelet counts. The mechanisms for the changes are not known, but it was suggested that these effects may contribute to the increased risk of clotting diseases in some alcoholics. Other factors that may be involved are the higher hematocrit (number of red blood cells) and the lower fibrinolytic activity (decreased dissolution of fibrin, the basic element of blood clots) seen in the blood of alcoholics.

### Possible Protective Effects of Moderate Alcohol Consumption

Although it is clear that heavy alcohol use is associated with several changes in cardiovascular physiology that may account for the increased incidence of CHD (Sundby 1967; Pell and D'Alonzo 1973; Wilhelmsen et al. 1973; Dyer et al. 1977; Shaper et al. 1981), there is some evidence that moderate alcohol consumption may protect against CHD. In a 1984 review of 11 studies, Rohan found that 7 of the studies suggested a reduced risk of CHD following moderate current alcohol consumption (Rohan 1984).

For example, in a study of factory employees in Chicago, Dyer et al. (1980) found, after controlling for age and smoking, that the incidence of CHD decreased with alcohol consumption of up to four to five drinks a day. However, in persons who consumed more than five drinks per day, the rates increased, which suggests a "U shaped" relationship between alcohol consumption and CHD death rates. The relationship between reduced incidence of CHD and moderate drinking has also been observed in case-controlled and longitudinal studies and in several ethnic populations from several different countries (Stason et al. 1976; Yano et al. 1977; Klatsky et al. 1979; St. Leger et al. 1979; Dyer et al. 1980; Laporte et al. 1980; Marmot et al. 1981; Marmot 1984).

It should be pointed out that in none of these studies was alcohol use associated with decreased mortality. In one study the lower mortality from CHD was offset by an increased mortality from cancer and stroke (Blackwelder et al. 1980).



In spite of the wide range of epidemiological studies that have suggested a protective effect of moderate drinking, most of this evidence has been recently questioned. For example, Eichner (1985) pointed out that in the Kaiser-Permanente study by Klatsky et al. (1974), the teetotalers, who were found to have a higher prevalence of CHD than the moderate drinkers, included not only lifetime abstainers but also ex-drinkers who might have quit drinking because of early signs of CHD. The inclusion of such ex-drinkers in the abstinent group would increase the prevalence of CHD in that group. Eichner also argues that the 464 subjects with infarction were those who survived their heart attack long enough to be admitted to a hospital, and this too would bias the results of the study.

Similar criticisms have been raised about other epidemiologic studies that suggest a protective effect of moderate or light drinking. It has been argued that light or moderate use of alcohol is less a biological modifier of processes involved in CHD development and more a marker of behavior and lifestyle patterns that are less conducive to heart attack. These patterns may include greater consciousness regarding diet, weight, exercise, and other health matters and less tendency to engage in the aggressive, competitive, and hard-driving behavior that is reported to be conducive to heart attacks (Castelli 1984).

Eichner (1985) has also questioned the mechanisms that have been proposed to account for the protective effects of moderate drinking. Studies have shown that alcohol increases the plasma levels of high density lipoproteins (HDL) that are thought to be protective against CHD and atherosclerosis. Further fractionation of the HDL class of lipoproteins has shown that alcohol consumption increases the concentration of only the most dense subfraction, HDL<sub>3</sub> (Goldberg et al. 1984; Haskell et al. 1984), while the HDL<sub>2</sub> subfraction, the fraction associated with protection against CHD (Miller et al. 1981; Ballantyne et al. 1982), is unchanged by alcohol.

It therefore appears to be premature to assume that moderate alcohol consumption provides protection against CHD. Also, the mechanisms proposed to explain the protective effects of alcohol may be invalid.

## EFFECTS ON THE ENDOCRINE AND REPRODUCTIVE SYSTEMS

Alcohol may have both direct and indirect effects on endocrine and reproductive system function. Alcohol affects every endocrine system (Cicero 1981), and, because hormones affect the cellular biochemistry of every organ system, the results of alcohol abuse spread far beyond its immediate toxic effects. This spreading of endocrine effects is largely due to the organization of endocrine glands into functional hierarchies called axes. For example, the hypothalamic-pituitary-gonadal (H-P-G) axis consists of the hypothalamus (an endocrine structure in the brain), the pituitary gland (located at the base of the brain), and the gonads. In the H-P-G axis, hormones secreted by the hypothalamus stimulate the pituitary to secrete certain hormones that affect the gonads, stimulating them to

secrete sex hormones. Because every endocrine axis has numerous feedback controls (Fink 1979), changes in one component of an endocrine axis (e.g., the hypothalamic component of the H-P-G axis or the hypothalamic-pituitary-adrenal axis) may affect other components (pituitary, adrenal, or gonadal) of that axis.

### Effects on the Hypothalamic-Pituitary-Adrenocortical Axis

Stress stimulates the hypothalamic-pituitary-adrenocortical (H-P-A) axis along with the sympathetic nervous system (McCann et al. 1971). Guaza et al. (1983) observed that acute alcohol administration to rats induced a significant rise in serum levels of the adrenal hormone, corticosterone, that appeared to be related to the blood alcohol concentration, whereas chronic alcohol administration in the form of a liquid diet did not alter the levels of serum corticosterone. It is extremely difficult to differentiate between stress-induced increases in the adrenal steroid secretion and similar effects caused by alcohol (Cicero 1981). It has been suggested that alcohol's effects on the H-P-A axis may be due to stress associated with its administration. Alcohol does not appear to act directly on the adrenals but seems to potentiate the action of the hypothalamus on the pituitary release of adrenal corticotrophic hormone (ACTH), which stimulates the adrenal cortex to produce its hormones.

In vitro studies of rat adrenal cells exposed to high concentrations of alcohol did not change the basal production of corticosterone by these cells, even though the alcohol concentrations used were high enough to have been lethal if they had been present in the blood of an intact animal. However, corticosterone production by these cells in response to ACTH stimulation was reduced in a manner that was clearly related to alcohol concentration, and this may have physiologic significance (Guaza and Borrell 1984).

The consequences of acute alcohol administration on the H-P-A axis are not yet well understood, but they seem to play some part in the development of tolerance and physical dependence (Sze 1975; Wood 1977; Tabakoff and Yuanai 1979). Rats that were chronically exposed to alcohol and rats that were previously dependent but are currently abstaining show tolerance to the stimulatory effects of alcohol on steroid hormone production in the pituitary-adrenal axis (Guaza and Borrell 1985). The results of these studies indicate that chronic alcohol treatment, which can produce dependence and tolerance, can induce changes in the response of adrenal hormones to alcohol that persist even after a period of complete abstinence. The findings may raise serious questions about the reversibility of the endocrinological effects of alcohol.

### Effects on the

### Hypothalamic-Pituitary-Thyroid Axis

The most consistently observed effects of alcohol on the hypothalamic-pituitary-thyroid (H-P-T) axis seem to be a modest decrease in the serum levels of the thyroid hormone thyroxine (T<sub>4</sub>) and a marked decrease in the serum



levels of the more active thyroid hormone triiodothyronine ( $T_3$ ). The effects are most pronounced in chronic alcoholics, particularly in the presence of alcoholic hepatitis or cirrhosis. The decrease in the levels of  $T_3$  appears to result from the effects of alcohol on a liver enzyme called a dehalogenase, which plays a major role in the conversion of  $T_4$  to  $T_3$  by catalyzing the removal of an atom of iodine from a molecule of  $T_4$ . In fact, it has been shown that the circulating level of serum  $T_3$  is inversely related to the extent of liver damage (Israel et al. 1979)—that is, the greater the liver damage, the lower the circulating level of  $T_3$ .

$T_3$  is one of the primary determinants of the rate of liver oxygen consumption. If  $T_3$  levels are low, reduced liver oxygen consumption should be expected. Paradoxically, however, livers in rats chronically treated with alcohol show *increased* rates of oxygen uptake, despite decreased circulating levels of  $T_3$  (Israel et al. 1975). This increase in oxygen uptake in the liver, termed "hypermetabolism" or a "hypermetabolic state," is thought to result in lowered levels of oxygen (hypoxia) in venous blood leaving the liver. This venous hypoxia, in turn, is proposed as a causative factor in the necrosis observed around the central vein of the liver after chronic ethanol consumption.

A hypermetabolic state in the liver has been observed after chronic and acute ethanol exposure in liver slices, hemoglobin-free liver perfusions, and in vivo (Israel et al. 1973; Thurman et al. 1976; Thurman and Scholz 1977; Sato et al. 1980; Ji et al. 1982; Bredfeldt et al. 1985). Other researchers, however, have observed no change in oxygen consumption in hepatocytes, hemoglobin-containing liver perfusion systems, and in vivo (Christensen et al. 1977; Gordon 1977; Cederbaum et al. 1978; Kondrup et al. 1979; Berry et al. 1980; Schaffer et al. 1981). These differences in experimental results have been attributed to various causes, such as hypoxic tissue preparation (in the case of liver slices and hemoglobin-free perfusions) and the use of rats that were too old at the start of chronic alcohol treatment (Britton et al. 1984; Stowell and Crow 1985). It is also uncertain whether these observations can be extrapolated to humans.

In baboons, dogs, and rats treated either acutely or chronically with alcohol, liver oxygen uptake was increased, but the portal blood flow was also increased, leaving tissue oxygenation unperturbed (Villeneuve et al. 1981; Baraona et al. 1983; Bredfeldt et al. 1985). However, the adaptability to low oxygen tensions such as those caused by respiratory depression may result in localized hypoxic tissue damage (Bredfeldt et al. 1985).

The antithyroid drug propylthiouracil (PTU) has been administered to both humans and rats on the assumption that alcohol results in liver hypermetabolism and that this condition contributes to alcohol-mediated liver damage. The principal action of PTU is to inhibit the dehalogenase activity of the liver, thereby decreasing the production of  $T_3$  (although it also mildly inhibits  $T_4$  secretion by the thyroid). Thus, it has been hypothesized that reducing the levels of  $T_3$  should reduce liver oxygen consumption and consequently eliminate the hypoxia around the central

vein. Experiments have shown that PTU blocks the increase in ethanol clearance rates in rats and blocks the hypermetabolism observed in hemoglobin-free perfusion systems (Ji et al. 1980; Yuki et al. 1982).

In human patients admitted to a hospital with a diagnosis of acute alcoholic hepatitis, it was found, paradoxically, that those admitted with the most liver damage, and consequently already having the lowest circulating levels of  $T_3$ , received the most benefit from treatment with PTU on admission (Orrego et al. 1979). Other researchers have failed to confirm even this paradoxical finding (Halle et al. 1982). Because the putative benefits of PTU were observed during abstinence from alcohol, it is possible that the drug may act through a mechanism independent of its known effect on dehalogenase.

## Effects on the Hypothalamic-Pituitary-Gonadal Axis

### *Endocrine Effects in Men*

Alcohol has effects on the hypothalamic-pituitary-gonadal (H-P-G) axis that may impair reproductive endocrinology and physiology (Cicero 1981). Alcoholic liver disease is commonly associated with failure of gonadal function in both men and women, even before the liver disease is advanced (Van Thiel et al. 1981; Van Thiel 1983a). This failure is thought to occur as a result of alcohol's toxic effects on various parts of the H-P-G axis. Hypoandrogenization (decreased levels of male sex hormones) is common in alcoholic men, 70 to 80 percent of whom show testicular atrophy and infertility after long-term alcohol abuse (Van Thiel et al. 1982). Testicular tissue from chronic alcoholic men shows atrophy of testicular tubules and loss of mature sperm cells (Van Thiel et al. 1974), and many of the less mature germ cells show abnormal morphology. Hyperestrogenization may also be present in men (see figure 2).

In the past, many of these endocrine dysfunctions have been considered consequences of alcoholic liver disease, but current studies indicate that the problems can be present in men with essentially normal livers and that a reduction in testosterone can be produced in normal volunteers after 72 hours of alcohol ingestion equivalent to about a pint of whiskey per day (Van Thiel 1983b). Additional studies have shown that alcohol or acetaldehyde added to the medium in which rat testes are perfused, at concentrations comparable to those seen in intoxication, will reduce testosterone production (Chiao et al. 1981). The decrease in circulating levels of testosterone is accompanied by increased activity of hepatic alcohol dehydrogenase, resulting from a decreased rate of degradation of this enzyme (Mezey and Potter 1985).

The interrelationship between liver disease and sexual dysfunction has been examined in alcoholic patients with and without liver disease as well as in nonalcoholic patients with different forms of liver disease (Cornely et al. 1984). Of 20 alcoholics with cirrhosis, 14 described a history of impotence; only 10 of 40 nonalcoholic cirrhotics had such a



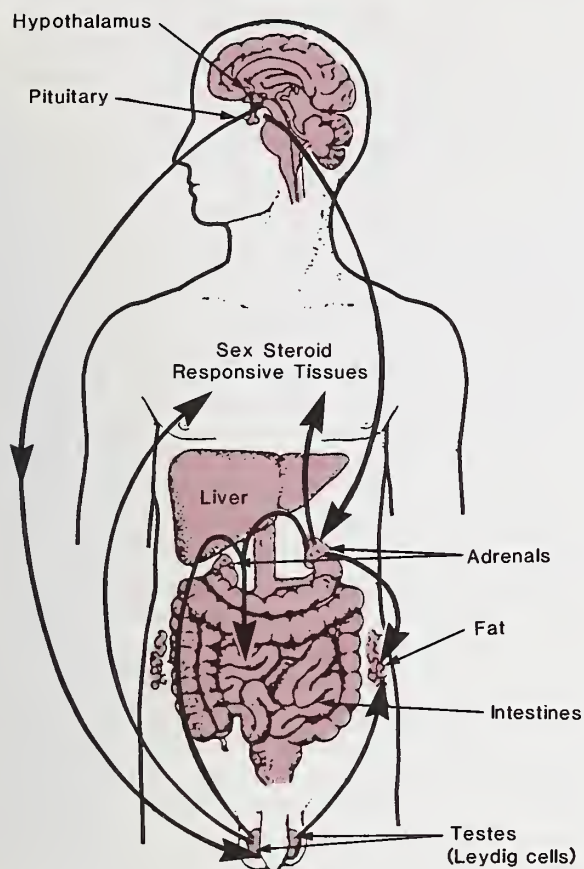


FIGURE 2. Hyperestrogenization resulting from alcohol consumption. Because several structures are involved in the physiologic pathways of sex steroid metabolism and action, ethanol can adversely affect hypothalamic-pituitary-gonadal function at a number of sites.

SOURCE: Van Thiel 1984, artwork by Nancy Lou Makris.

history. Also, although the nonalcoholic patients were more severely ill, the degree and the duration of impotence were greater in the alcoholic patients. These findings are thought to support the hypothesis that inhibition of testosterone production and secretion by the testes is principally responsible for impotence in alcoholic liver disease.

The effects of alcohol on plasma testosterone levels in otherwise healthy alcohol-dependent men have been examined in carefully controlled research ward studies (Mendelson et al. 1978). A significant dose-dependent decrease in plasma testosterone levels occurred in male alcoholics during a 10-day period of self-determined alcohol administration. Plasma testosterone levels decreased significantly in seven alcoholics, and plasma testosterone levels were lowest when blood alcohol levels were highest. However, abstinent alcoholic men studied under identical conditions had no significant changes in plasma testosterone levels (Mendelson et al. 1978). The decrease in plasma testosterone levels found in alcoholics during drinking is consistent with other data indicating that chronic alcohol intake depresses plasma testosterone levels in alcoholics (Mendelson and Mello 1974).

Chronic alcoholic men may also be "feminized," with female hair patterns and gynecomastia (breast enlargement). Normal to near-normal estrogen levels are found along with androgen deficiencies, which suggests that feminization results from the direct toxic effects of alcohol as well as the indirect effects of liver disease (Johnston et al. 1981). Van Thiel et al. (1985) report that the metabolic clearance of estradiol in these men is normal, and they question whether recently discovered phytoestrogens (nonsteroidal estrogenic materials of plant origin that have been found in alcoholic beverages) may accumulate in the plasma of alcoholic men.

Alcohol has been shown to have significant effects on the production of luteinizing hormone (LH). LH, a hormone secreted by the pituitary gland, stimulates progesterone secretion in females and testosterone secretion in males. In rats, both acute injections of alcohol and chronic alcohol administration severely depressed serum LH values (Chapin et al. 1980; Cicero 1980). Administration of ethanol and other alcohols to rats via inhalation at doses equal to the current threshold limit values in industry significantly reduced levels of circulating testosterone after 6 hours of exposure but had no effect on LH levels; normal testosterone levels were restored after 18 hours of recuperation (Cameron et al. 1985). In humans, different studies have had different results: increases, decreases, and no changes in serum LH values have been seen, although most studies indicate that alcohol does not decrease LH in humans.

As testosterone levels increase, they have an inhibitory effect on the production of new LH. Conversely, serum LH values normally rise markedly when testosterone levels are low. Thus, LH levels normally are regulated by a rise or fall in testosterone levels (negative feedback mechanism). However, in studies where testosterone levels were reduced by alcohol, LH values increased only slightly, suggesting that alcohol directly inhibits the release of LH (Cicero 1981). Further studies have substantiated this, showing an alcohol-induced depression of LH levels in castrated animals (Redmond 1980). Involvement of the hypothalamus in this phenomenon is indicated by recent studies showing that LH-releasing hormone (LH-RH), a hypothalamic hormone that stimulates LH production, can overcome alcohol's depression of LH levels (Chapin et al. 1980; Redmond 1980).

Van Thiel (1983b) has suggested the following hypothetical mechanism: Alcohol, a direct gonadal toxin that does not need to be metabolized to be toxic, initially damages the Leydig cells of the testes, thereby reducing testosterone levels. Studies with perfused testes or cultured rat Leydig cells show that acetaldehyde, the metabolic product of ethanol, also affects the function of these cells. In a compensatory response, the hypothalamus and pituitary initially increase their secretion of LH to stimulate the production of more testosterone. This compensatory response fails with further alcohol exposure, however, and testicular and central gonadotropic secretion defects develop. At some point between the initial effects and the development of testicular atrophy, these changes in the testosterone-producing Leydig cells become irreversible.



Recent studies by Mello et al. (1985) support the suggestion that the acute testosterone-lowering effects of alcohol in men occur primarily in the testes. In experiments using male Macaque monkeys, these investigators demonstrated that LH levels either remained the same or increased after testosterone levels fell, indicating that suppression of testosterone production was not taking place at the hypothalamic and pituitary levels.

Sex steroids, particularly testosterone, are produced in the fetal stage and are essential for male sexual differentiation (Bardin and Catterall 1981; Wilson et al. 1981). It has been suggested that androgens produced by the fetal testes bind to receptors at the hypothalamic level and are then converted to estrogens. In the fetus, these estrogens determine the characteristic adult male neuroendocrinologic and behavioral patterns. In a recent study, Parker et al. (1984) exposed developing rodent fetuses to alcohol in utero and during the neonatal period. The male pups showed reduced masculinization during the newborn period as well as for a period after weaning. This was evident in adult animals as reduced plasma testosterone levels and testicular mass, as well as reduced sexual motivation and behavior.

### *Endocrine Effects in Women*

Alcohol affects human male and female hormones differently (Mendelson et al. 1981; Mello et al. 1985). Although some investigators (Bhalla et al. 1976) have suggested that the mechanisms of endocrine failure in men and women are probably similar, recent studies found that alcohol does not suppress the female hormone estradiol, whereas both acute and chronic alcohol administration result in dose-dependent suppression of the male hormone testosterone (Mello et al. 1983).

Nonetheless, menstrual disturbances, loss of secondary sex characteristics, and infertility are seen in alcoholic women. Chronic alcohol abuse disturbs H-P-G function, resulting in early menopause, lower postmenopausal gonadotropin levels, and increased levels of the female sex hormones estrone and estradiol (Van Thiel et al. 1985). However, acute alcohol administration did not produce any changes in LH levels in menopausal women (Mendelson et al. 1985).

A recent study (Wilsnack et al. 1984) presented extensive data on drinking and reproductive system function from a representative national sample of women (see also the section on women in chapter I). In this sample of 917 women, dysmenorrhea, heavy menstrual flow, and premenstrual discomfort increased with drinking level. Women who consumed at least 1½ ounces of pure alcohol every day had elevated rates of gynecological surgery other than hysterectomy. Other obstetric disorders, such as miscarriage, stillbirths, and premature births, showed significant elevations at the upper levels of drinking, but, surprisingly, the elevations were not so great among women drinking at those upper levels as they were among light drinkers classed as "temporary abstainers"—women who had previously been infrequent drinkers and reported alcohol consumption in the past 12 months but not in the

past 30 days. The temporary abstainers were the most likely of all the women to report gynecologic and obstetric problems. Another surprising finding was that hysterectomy was less common in women who consumed an average of 2 ounces or more of alcohol a day.

Three possible explanations were offered for the higher frequency of gynecologic and obstetric problems among the temporary abstainers (Wilsnack et al. 1984): (1) women who already have gynecologic dysfunction, perhaps because of hormonal disturbances, might find alcohol unpleasant and therefore tend to abstain from it, at least temporarily; (2) temporary abstainers may be especially health conscious, and this health consciousness may be reflected in both a greater disposition to abstain from alcohol and an unusual attentiveness to possible medical problems; and (3) women with gynecologic problems may have been advised by their physicians or may have decided on their own to limit the use of alcohol. Any one of these alternatives could explain the overrepresentation of women with gynecologic or obstetric problems among the temporary abstainers. Wilsnack et al. (1984) also suggest that the lower rate of hysterectomy among women averaging 2 ounces or more of alcohol a day could have been a reflection of a tendency among heavier drinkers to ignore or minimize various menstrual symptoms that might be indicators of a need for hysterectomy. It is highly unlikely, in view of the known effects of alcohol on reproductive and endocrine function, that alcohol had any "protective" effect against gynecologic or obstetric disorders.

Only recently have efforts been made to understand the interplay between the complexities of the female reproductive system and alcohol consumption. Some studies indicate that the phases of the menstrual cycle may influence the behavioral and biological effects of alcohol. However, more recent studies both with women (Mello et al. 1984a) and female monkeys (Mello et al. 1984c) have indicated that peak blood alcohol levels did not differ significantly in the various phases of the menstrual cycle.

Studies by Mendelson et al. (1981) have shown that low doses of alcohol, producing a blood alcohol level (BAL) of 88 mg/dL (the legal definition of intoxication in most States is 100 mg/dL), had no significant effect on estradiol in six women. Mello et al. (1983) have studied the effects of high doses of alcohol on pituitary and gonadal hormones in female Macaque monkeys. The doses of alcohol administered to these animals produced BALs comparable to those often observed in alcoholic men. These high doses of alcohol produced no significant changes in pituitary or gonadal hormones in female rhesus monkeys, but female animals given high doses of alcohol showed changes in the luteal phase of their menstrual cycle that may be related to first-trimester spontaneous abortions seen in alcoholic women (Mendelson and Mello 1985).

Because decreased ovarian mass has been seen with chronic intoxication, it is suggested that sustained, chronic alcohol intoxication may be necessary to affect the female pituitary and gonadal hormones (Jung and Russfield 1972). Mello et al. (1984b) produced chronic alcohol intoxication in female Macaque monkeys that self-administered alcohol



and therefore self-controlled their alcohol dosage. At these high chronic doses, pathological changes were seen in the pituitary, uterus, and ovaries. Amenorrhea (absence of menstruation) and reproductive system pathology appeared to be due to chronic intoxication and not to malnutrition or liver disease. Lower doses of alcohol did not affect normal menstrual function.

The difference in the acute effects of alcohol on the reproductive hormones in men and women may be related to a sex-linked difference in responsiveness to alcohol. For example, whereas women appear to be more sensitive to alcohol-related liver disease, men appear to be more sensitive to the acute effects of alcohol on the H-P-G axis (Mello et al. 1983). The mechanisms and many of these effects themselves are not understood, and current research continues to seek clarification.

## ALCOHOL AND OTHER DISORDERS

Along with the systems discussed here, alcohol is known to affect the central nervous system (see chapter III), the skeletal muscle (myopathy), the pancreas (pancreatitis), the hematopoietic (blood forming)-system (anemias), and the respiratory system. The effects on these systems have been presented in detail elsewhere (Lieber 1982a; Pattison and Kaufman 1982; Geokas 1984). This section focuses on nutritional and metabolic disturbances associated with alcohol use.

### Nutritional Disturbances

Two recent studies have presented details of the relationships of alcohol consumption to diet and health status (Lieber 1984a; Hillers and Massey 1985). Hillers and Massey (1985) quantified long-term alcohol intake in a group of middle-class men. There was a tendency for calories from protein, fat, and carbohydrate to decrease as the number of calories from alcohol increased. The overall quality of the diet declined. An overall decrease in fiber, protein, calcium, iron, vitamins A and C, and thiamine intake was reported. A large percentage of the men with the highest intake of alcohol reported eating less food and skipping meals altogether.

Alcohol remains a common cause of malnutrition through reduction of food intake (primary malnutrition) and through the direct effects of alcohol on the gastrointestinal tract that produce malabsorption and maldigestion (secondary malnutrition) (Lieber 1984b). Deficiencies in thiamine, folate, pyridoxine, vitamin A, and zinc are common in alcoholics, and plasma amino acids are also found to be abnormal in alcoholic patients with liver disease (Wu et al. 1955). Plasma branched-chain amino acids and alpha-amino-n-butyric acid are thought to be affected by two other variables in alcoholics: dietary protein deficiency and advanced cirrhosis.

Rats given ethanol as 36 percent of total calories (Shank et al. 1984) were found to consume nearly one-third less food than rats fed a 20 percent ethanol diet, although the average daily ethanol consumption of the two groups was not significantly different. Animals given the 36 percent

ethanol diet gained markedly less weight than animals fed the 20 percent ethanol diet. In the 36 percent ethanol group, the nutritional deficit appeared to affect the pituitary-thyroid axis (see also the section on the Effects on the Endocrine and Reproductive Systems in this chapter).

In 41 patients with alcoholic liver disease (Majumdar et al. 1982), biochemical evidence of thiamine deficiency was observed in all subjects. Riboflavin deficiency was detected in patients with histologically normal liver but not in others. All patients were found to be deficient in pyridoxal-5-phosphate, which is metabolically derived from vitamin B<sub>6</sub>. Serum folate was decreased in all patients except those with alcoholic hepatitis. Vitamin B<sub>12</sub> levels were raised in cirrhotics. Because these biochemical changes in blood vitamin status may precede clinical signs of a disease process, they may have prognostic value.

### Metabolic Disturbances

Studies of alcoholics have indicated a reduction in bone mass in various parts of the body, including the iliac crest (hip), the neck of the femur (thigh bone), and the calcaneus (heel bone) (Bikle et al. 1985). Drinking alcoholic beverages has also been implicated as a risk factor in osteoporosis in men.

The effects of alcohol on metabolism of carbohydrates and fat depend on the nutritional state of the person, as do the effects on free fatty acids and on a group of compounds known as ketone bodies that are produced during the oxidation of fatty acids (Arky 1984). Alcohol produces a brief rise in blood sugar in well-nourished persons, but it may produce a drop in blood sugar in persons who have fasted 24 hours or more. When alcohol is ingested by persons who have not eaten for 24 hours or more and whose livers are depleted of glycogen, hypoglycemia (abnormally low blood sugar level) may result, with potential for coma and death.

Insulin-dependent diabetics are most vulnerable to both hypoglycemia and ketoacidosis (a disturbance in the acid-base balance caused by excessive accumulation of ketone bodies) because of alcohol's hypoglycemic action (Arky 1984). Patients with unstable insulin-dependent diabetes should be cautioned against using alcoholic beverages.

## THE IMMUNE SYSTEM

### Immune Function in Alcoholic Patients

Chronic alcohol abuse is associated with enhanced susceptibility to several infectious diseases and certain types of cancers (see table 1). This association suggests that the ability to recognize or combat foreign agents is severely compromised in alcoholics. In fact, several immune deficiencies have been observed in alcoholics at the time of admission for treatment. For example, 4 to 8 percent of admitted patients have decreased circulating levels of white blood cells called neutrophils, indicating that the ability to phagocytize (engulf) bacteria is reduced (Lieber et al. 1979; Tuyns 1979).



TABLE 1. *Infectious diseases and cancers observed with increased frequency in alcoholics*

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Tuberculosis (Smith and Palmer 1976)
Pneumonia (Bomalaski and Phair 1982)
Yellow fever (Bomalaski and Phair 1982)
Cholera (Bomalaski and Phair 1982)
Bacteremia (Bomalaski and Phair 1982)
Bacterial peritonitis (Bomalaski and Phair 1982)
Head and neck cancer (Kissin et al. 1973; Lieber et al. 1979; Tuyns et al. 1979)
Hepatitis B (MacSween et al. 1980)

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Also, the increase in the level of circulating neutrophils that is normally observed after a challenge with a bacterial toxin is weaker in alcoholics, reflecting a decreased marrow reserve of these cells (Tuyns 1979; Lieber et al. 1979). Other white blood cells called macrophages show decreased migration velocity to a site of infection and decreased adherence to foreign substances in alcoholics (Guarneri and Laurenzi 1968; Rimland and Hand 1980; Rimland 1983). These cells are involved in the phagocytosis and clearing of bacteria and other particles from the lungs, blood, and peritoneum (the lining of the abdominal cavity). Injected particles of aggregated serum albumin are cleared from the circulation of alcoholics more slowly than is the case in nondrinkers, perhaps reflecting the functional deficiencies of the alcoholics' macrophages (Liu 1979).

Lymphocyte function is also reduced in alcoholic patients. Lymphocytes are white blood cells involved in cell-mediated immunity, a function that can be assessed by certain skin tests. Alcoholics have fewer and smaller reactions to such skin tests than nonalcoholic patients (Berenyi et al. 1974; Snyder et al. 1978; Bjorkholm 1980). This decrease in cell-mediated immune function may account for the higher incidence of tuberculosis and head and neck cancers associated with Epstein-Barr virus (see table 1). The circulating level of lymphocytes is also reduced in some patients (Lieber et al. 1979; Tuyns 1979).

Alcoholics also have abnormal responses of the humoral immune system, a system that functions by producing antibodies (protective proteins) in response to invading bacteria and other antigens. Antibody response to an antigen that has not been previously encountered is decreased in alcoholics (Gluckman et al. 1977). Also, there is immunoglobulinemia (persistently elevated blood levels of immunoglobulins, a class of protein that includes antibodies), suggesting that many antibody-producing cells are responding to a persistent antigenic challenge (Wilson et al. 1969). High titers of antibodies to *Escherichia coli* bacteria, normally present in the human intestine, suggest that the normal intestinal barriers to these organisms may be broken by chronic exposure to alcohol (Thomas et al. 1973).

### Direct or Acute Effects of Alcohol on Immune Function

Observed immune deficiencies in alcoholics and the attendant increase in morbidity may be attributed to lifestyle, liver disease, poor nutrition, or poor absorption of

nutrients (see the Intestine and the Nutritional Disturbances sections of this chapter) as well as to alcohol itself. To investigate the direct effect of alcohol on various components of the immune defense system, studies have been carried out on the acute effects of alcohol in healthy human volunteers as well as on the effects of acute and chronic exposure in animals and in cell culture systems.

Acute alcohol treatment with intoxicating alcohol doses in humans and rabbits has been shown to inhibit the mobilization of neutrophils (Brayton et al. 1979; MacGregor and Gluckman 1979). Also, the ability of neutrophils to adhere to nylon fibers is decreased after alcohol treatment (MacGregor et al. 1974). Both effects suggest that acute exposure to alcohol can impair defenses against bacteria. In support of this concept, it has been shown that intoxicated animals have reduced capacity to survive an acute bacterial challenge (Buckley et al. 1978).

Acute intoxicating doses of alcohol also decrease the ability of animals to clear aerosolized bacteria from the lungs (Green and Kass 1964). Although this problem may reflect depression of respiratory system cilia (filamentary cellular projections whose motion propels particulate matter out of the respiratory tract) or decreases in surfactant secretion, the problem may also be related to depressed alveolar macrophage function (Okeson and Divertie 1970; Bomalaski and Phair 1982). Macrophage migration into the lung, as well as phagocytosis and bactericidal activities, are depressed by alcohol (Guarneri and Laurenzi 1968; Rimland and Hand 1980). Application of alcohol to macrophages in vitro produces a refractory state that inhibits the respiratory burst associated with bactericidal activity (Dorio et al. in press). This indicates that alcohol may have a direct effect on the particulate-clearing properties of macrophages.

Although chronic alcohol consumption decreases the response to skin tests that measure delayed hypersensitivity, acute doses of alcohol or chronic doses in a controlled environment appear to have no effect (Spagnuolo and MacGregor 1975). In humans, deficits in cell-mediated immunity are associated with alcoholic hepatitis and not with cirrhosis (Snyder et al. 1978). In rats, sensitization to dinitrofluorobenzene was impaired after 3 months of an alcohol treatment that was sufficient to produce fatty infiltration of the liver (Tennenbaum et al. 1969). In guinea pigs, alcohol treatment for 5 weeks decreased the response of lymphocytes to mitogens (chemicals that stimulate cell multiplication) (Roselle and Mendenhall 1984). Similarly, the application of alcohol to lymphocytes in vitro has been shown to decrease blastogenesis (cell multiplication) in response to mitogens as well as spontaneous, antibody-dependent, cell-mediated cytotoxicity (Stacey 1984; Glassman et al. 1985). With the exception of the effects in culture, the observed deficits in cell-mediated immunity in alcoholic humans appear to require long-term exposure and may be related to alcoholic liver disease rather than direct effects of alcohol itself.

In contrast to the apparent lack of an acute effect of alcohol on cell-mediated immune function, healthy human volunteers drinking in a controlled environment and rats



treated with alcohol have a sluggish antibody response to new antigens (Tennenbaum et al. 1969; Loose et al. 1975; Gluckman et al. 1977). However, the secondary antibody response in previously immunized animals was unimpaired (Tennenbaum et al. 1969; Loose et al. 1975). Alcohol appears to have a direct effect on the body's ability to form antibodies to new antigens.

Acute and chronic doses of alcohol have been shown to suppress all arms of the immune defense system, and it seems likely that these effects are involved in the increased susceptibility of alcoholics to infectious diseases. It is not yet established that alcohol is involved in the progression of disease in persons who have been infected with the virus responsible for acquired immunodeficiency syndrome (AIDS) (NIAAA in press). The AIDS virus, also known as human immunodeficiency virus (HIV), human T-lymphocyte virus (HTLV-III), or lymphadenopathy-associated virus (LAV), produces a catastrophic infection of the T-lymphocytes and failure of immune function.

## ALCOHOL AND CANCER

Of all medical conditions with which alcohol is associated, cancer demonstrates as much as any other the complexities and wide range of alcohol's actions. Studies have indicated that alcohol use increases the risk of many cancers (see table 2) (Lieber et al. 1979). Several factors may be operating in the susceptibility to cancer. For example, alcohol-mediated immunodeficiency may reduce the ability to defend against cells with foreign antigens or against viruses such as the Epstein-Barr virus, which is thought to cause cancers of the head and neck (see the section on the Immune System in this chapter). Also, nutritional disturbances, including deficiencies in thiamine, folic acid, vitamin A, riboflavin, and pyridoxine, have been observed in alcoholics (see the section on Nutrition in this chapter). These deficiencies increase the incidence of some types of cancer in animals. Finally, alcohol can induce any of several microsomal enzymes, including cytochrome P<sub>450</sub>, that are responsible for activating procarcinogens to carcinogenic compounds. These activated compounds may then react with cellular components such as deoxyribonucleic acid (DNA) or the enzymes involved in the maintenance or expression of DNA, resulting in a genetically altered cell (see figure 3).

The involvement of microsomal enzymes that are induced by alcohol has been supported by a number of

TABLE 2. *Alcohol-related tumors*

Oral cavity
Tongue
Pharynx
Larynx
Esophagus
Stomach
Liver
Lung
Pancreas
Colon
Rectum

studies on chemical carcinogenesis (Lieber et al. 1979). These effects have been seen in many species, including humans, and in many tissues. Also, the enzymes induced by chronic ethanol consumption are involved in the metabolism of many drugs and carcinogens (Farinati et al. 1985; Seitz 1985). Farinati et al. (1985) studied the effects of alcohol consumption on the activation of the smoking- and diet-associated procarcinogen nitrosopyrrolidine. Chronic ethanol exposure significantly increased the ability of liver, lung, and esophageal tissue from Sprague-Dawley rats to activate nitrosopyrrolidine.

Swann and colleagues (Swann 1984; Swann et al. 1984) have found that ethanol alters the distribution of carcinogenic nitrosamines in rats. Alcohol impairs the absorption of small oral doses of dimethylnitrosamine by the liver, thereby increasing the exposure of sensitive organs outside the liver to this carcinogen. Examination of urinary excretion indicates that alcohol may also inhibit clearance of dimethylnitrosamine in humans. Kellermann et al. (1973) have also shown a relationship between activity of the microsomal enzyme benzo(a)pyrene (BP) hydroxylase and tumor formation. In the liver, enhanced activation of procarcinogens by BP hydroxylase (in females) and dimethylnitrosamine demethylase (in both males and females) was observed after ethanol administration (Seitz et al. 1981). The results indicate that chronic ethanol consumption significantly affects microsomal enzyme activities in liver and other tissues, apparently increasing the capacity of these tissues to activate potentially carcinogenic compounds.

A recent case-control study comparing cancer cases indicates that alcohol abuse and, less strongly, smoking are associated with increased risks for cancers of the oral cavity, pharynx, and larynx (Elwood et al. 1984). In this study, 374 patients with primary epithelial cancers in one or another of these sites were studied. The controls were patients with selected other cancers, matched for age and sex. The findings in this study suggest that alcohol and tobacco smoke make independent and different contributions to the development of these cancers. A third relevant factor was socioeconomic circumstances, and in these diet may play a causative role.

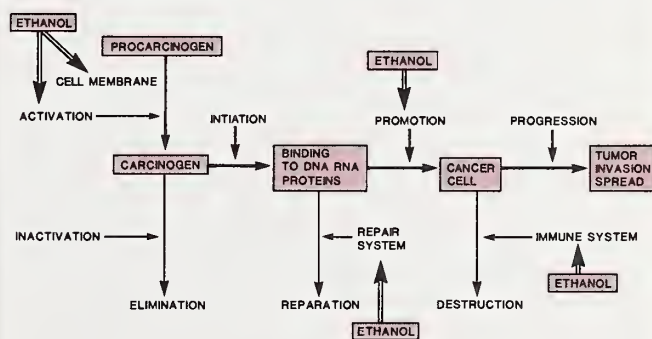


FIGURE 3. Simplified scheme of two-step carcinogenesis and possible sites of action of ethanol.

SOURCE: Seitz 1985.



## CELLULAR MECHANISMS OF ALCOHOL DAMAGE

A fundamental question raised by the multiplicity of systems affected by alcohol and the great range of diseases caused by alcohol is this: How can a simple organic molecule, ethyl alcohol, to which we are exposed almost exclusively by drinking cause such diverse consequences? Is it reasonable to think that damage in the liver, the brain, the heart, and many other organs arises from a different mechanism in each site? Or is it more likely that there is a common cellular mechanism of alcohol damage in all these sites? Recent hypotheses emphasize the latter possibility.

One hypothesis is that acetaldehyde, the toxic metabolite of alcohol, may be the proximate cause of alcohol toxicity at the cellular level throughout the body. However, it has been argued that the acetaldehyde mechanism cannot account for the extensive array of injury caused by alcohol throughout the body, because acetaldehyde does not increase to levels that seem likely to produce much toxicity. This is particularly true outside the liver (Taraschi and Rubin 1985). Consequently, other putative mechanisms are attracting attention. Among these is the hypothesis that the cell membranes are a more likely site of primary damage from alcohol, and that damage to those membranes is caused primarily by alcohol itself, not by acetaldehyde.

It has long been known that alcohol molecules, being lipid soluble, can penetrate cell membranes and commingle with the lipid and protein molecules that are their principal constituents. The anesthetic properties of alcohol, for example, have been attributed to the occurrence of such penetration in the membranes of nerve cells in the brain. There is no evidence that alcohol molecules bind to specific receptor sites on nerve cell membranes; instead, the penetration is rather general throughout the cell membranes, and a major result is impairment of neurotransmission, a membrane phenomenon.

More than simple perturbation of membranes is involved, however. Biological membranes consist of a double layer of lipids, and this bilayer serves as a matrix for membrane proteins that perform functions vital to the cell, especially the transport of important substances into and away from the cell (Singer and Nicholson 1972). Some of the membrane lipids are essential for the functioning of these membrane proteins. Disturbance of these membrane lipids by the penetration of alcohol can thus interfere with membrane-bound enzymes, and the consequences can affect overall cell function.

Furthermore, cell membranes appear to be very similar in cells throughout the body as well as in different species. Michaelis and Michaelis (1983) reported that the acute effects of ethanol on the chemical and physical properties of cell membranes are essentially the same in all species and are similar in different types of cells in different organs.

Taraschi and Rubin (1985) have observed that alcohol reduces the activities of certain enzymes that are embedded in the cell membrane, apparently because alcohol has a disruptive effect on the integrity of the membranes. In

studies with mitochondria (subcellular particles responsible for the cell's respiration, a process that occurs in the mitochondrial membranes), these investigators have also demonstrated that alcohol treatment may both reduce the synthesis of certain membrane-bound proteins and impair the incorporation of those proteins into the mitochondrial membrane. In addition, Thayer and Rubin (1979) found that mitochondrial fragments isolated from rats chronically exposed to ethanol had decreased respiration rates.

## SUMMARY

The range and complexity of alcohol's effects on the body are immense. Virtually every organ system in the body is affected by alcohol, either directly or indirectly.

Our understanding of the medical consequences of alcohol continues to expand. However, new knowledge about the processes of liver cirrhosis; the effects of alcohol on the digestive, cardiovascular, endocrine, and many other systems; and the role alcohol plays in cancer and immune system dysfunction are all parts of a complex picture puzzle that still has many missing pieces.

A major gap in the picture is understanding of fundamental mechanisms that can explain the enormous range of alcohol's effects throughout the body. Are only a few basic cellular mechanisms involved in all the diverse effects of alcohol? Do these mechanisms start with interactions between alcohol and cell membranes? Some recent evidence cited in this chapter supports that possibility, but much more study of cell and membrane biochemistry and physiology is needed to answer this question. Better understanding of basic cell structures, of alcohol's effects on those structures, and of the interaction between cell structure and cellular function may lead to a more productive understanding of the diverse disorders associated with alcohol abuse and alcoholism.

Although the basic mechanisms of alcohol's varied effects throughout the body are not yet fully understood and respected and accomplished researchers still have differences of opinion in many areas, there is growing optimism in the field that enough pieces of the complex picture may soon fall into place to allow significant advances in the treatment and prevention of alcohol-related pathologies.

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# Fetal Alcohol Syndrome

## and Other Effects of Alcohol on Pregnancy Outcome

Wide recognition of the fetal alcohol syndrome (FAS), a distinct pattern of physical and behavioral anomalies in the children of alcoholic women who drank heavily during pregnancy, came in the late 1960s and early 1970s with the publication of case reports from France (Lemoine et al. 1968) and the United States (Jones and Smith 1973; Jones et al. 1973). Because details of the earlier research on FAS have been presented in the *Fifth Special Report to the U.S. Congress on Alcohol and Health*, the older reports are not cited here unless they relate to newer findings.

This chapter discusses selected new research reports on the effects of alcohol on prenatal and postnatal development and the mechanisms underlying these effects. Because the literature on alcohol and pregnancy is vast—with scores of papers published annually on the subject and with more than 3,000 such papers published in the last 15 years—the chapter is necessarily highly selective. Regrettably, it is not possible to include all the important current work, and no claim of comprehensiveness is made. The chapter can only be a “sampler” that provides the reader with a sense of the major currents in this field and an understanding of some of the important and interesting findings that have been made recently.

### OVERVIEW

All the studies described in this chapter, and many others not cited, lead to the conclusion that substantial progress is being made in understanding the effects of prenatal alcohol exposure on the developing organism. Specific brain structures are being identified that are especially sensitive to alcohol and are involved in functions known to be impaired in the fetal alcohol syndrome. Knowledge of the subtle effects of maternal social drinking on the developing infant is growing. Factors that modify the risk of an alcoholic woman giving birth to a baby with the fetal alcohol syndrome are being discovered. Stages of pregnancy at which the embryo or fetus is especially vulnerable to alcohol are being identified. Scientific attention is being given to subpopulations that appear to be especially vulnerable to alcohol-related birth defects, an area of inquiry that can lead to more effective prevention efforts. And interesting new leads are being explored to understand underlying mechanisms. The research described in this chapter clearly shows that the study of alcohol-related birth defects has come a long way since the early 1970s, when the literature on this subject consisted mostly of FAS case reports.

The chapter begins with a review of findings from recent studies of the children of alcoholic mothers, including a 10th-year followup examination of several of the FAS infants first described by Jones and Smith (1973) and colleagues (Jones et al. 1973); a study showing an extraordinarily high FAS incidence in some American Indian populations; and a study that has identified several maternal factors, in addition to high alcohol intake, that contribute significantly to the risk of FAS. This review is followed by discussion of recent research to examine the more



subtle effects of lower, "social" levels of maternal drinking on offspring. The chapter concludes with a survey of some recent experimental studies of FAS in animal models, aimed at understanding dose-response and temporal factors in prenatal alcohol damage, neurobehavioral anomalies, and the underlying mechanisms of alcohol-related birth defects.

## THE CHILDREN OF ALCOHOLIC MOTHERS

### The Original FAS Children 10 Years Later

Two reports by Jones and Smith (1973) and colleagues (Jones et al. 1973) described a number of gross physical deformities in 11 very young children of severely alcoholic mothers who drank during pregnancy. The children all showed a similar pattern of craniofacial, limb, and cardiovascular defects, as well as growth deficiency and developmental delay. The facial and cranial deformities included short palpebral fissures (small eye openings), ptosis (drooping eyelids), microphthalmia (small eyes), midfacial hypoplasia (underdeveloped midface), epicanthal folds (skin folds across the inner corners of the eyes, which are abnormal in Caucasians), underdeveloped philtrum (the depression just above the upper lip), abnormally shallow notch in the upper lip "Cupid's bow"), an exaggerated space between the nose and the upper lip, and small head circumference. Abnormal palmar creases and minor joint abnormalities were also noted, and several of the children had cardiac defects, small hemangiomas (benign tumors consisting of dilated blood vessels), and minor ear anomalies.

Ten years later, 8 of these 11 children, some of whom are now teenagers, were reexamined (Streissguth et al. 1984a, 1985). (Two of the original group had died and one could not be located.) The findings of this study attest to the lasting consequences of heavy drinking by pregnant women.

Four of the eight children are in the borderline-retarded to low-normal range of intelligence (IQs of 70 to 86) but have attended regular classes supplemented with remedial education. The other four, with IQs ranging from 20 to 57, are severely retarded and have been in special classes. An earlier study of these children when they were much younger noted that the degree of intellectual impairment was correlated with the severity of malformation and growth deficiency (Streissguth et al. 1978). This correlation has persisted.

The physical characteristics of these eight children remain similar to those initially reported in 1973, although facial appearances have been altered somewhat by increased growth of the chin and nose. All the children remain below average in height, weight, and head circumference, but there has been improved weight gain with age. A number of new physical problems are evident that were not observed in the initial studies. These include chronic middle ear infections with sustained hearing loss, severe dental malocclusions, and vision problems. Although cardiac defects were noted in most of these chil-

dren in 1973, they have not been a major medical problem.

Two of the children continue to live with their natural mothers. The mothers of three children, who were among the four most severely handicapped, died of alcoholism within 6 years after the children were born, which suggests to these investigators that biological factors associated with the terminal stages of alcoholism may have contributed to the severe handicaps in these children. Two of the most severely handicapped children lived in stable foster homes, which leads the investigators to suggest that the quality of the later home environment does not ameliorate the damage caused by prenatal alcohol exposure. However, stable home environments did produce improvements in social and emotional development.

### Prevalence of FAS

Firm national data on FAS prevalence are as yet unavailable, although prevalence figures have been obtained for various localities. The most common estimate of overall FAS prevalence continues to be 1 to 3 cases per 1,000 live births, the range cited in the *Fifth Special Report*. This estimated range is based on reports from various American and European cities. The local reports have varied widely, depending on the location and the population under study. Thus, for U.S. cities, reported prevalence of FAS ranges from 0.4 per 1,000 in Cleveland (Sokol et al. 1980) to 1.3 per 1,000 in Seattle (Hanson et al. 1978) to 2.1 per 1,000 in Boston (Rosett et al. 1983). Estimates from Europe range from 1.6 per 1,000 in Sweden (Olegard et al. 1979) to 1.4 per 1,000 in France (Dehaene et al. 1981). Measurements of FAS prevalence that are limited to the offspring of women who are alcohol abusers are higher and more consistent, ranging from 23 to 29 cases per 1,000 births (Hanson et al. 1978; Sokol et al. 1980; Rosett et al. 1983). Recent evidence also indicates that some racial and cultural groups—blacks and certain American Indian tribes, for example—are at greater risk of FAS than the population as a whole.

Recently, there has been growing interest in assessing the incidence of FAS in specific subgroups in the population. In 1979 a project on FAS in Indian populations was inaugurated by the Indian Health Service (May and Hymbaugh 1983). One component of the project was a study of the epidemiology of FAS among American Indians. Data from the project on the incidence of FAS among three tribal cultures of the Southwest have recently been published (May et al. 1983).

The study, which provided a unique opportunity to determine the magnitude of fetal alcohol problems in well-defined populations, took place in 1982–1983 among Indians of New Mexico, southern Colorado, southern Utah, and northern Arizona who resided on 26 reservations with a total population of approximately 240,000. Three distinct cultural and social traditions are represented in the study population: the Pueblo, the Navajo, and the Plains culture (represented by the Apache and Ute Tribes).

The prevalence of FAS varied widely among these three cultural groups, ranging from 1.4 cases per 1,000 births for



the Navajo, to 2 per 1,000 for the Pueblo, to 9.8 per 1,000 for the selected Plains culture tribes. The overall prevalence of mothers who have ever given birth to fetal alcohol children is 6.1 per 1,000 women of childbearing age (range 4 to 33 per 1,000), and 25 percent of mothers who had given birth to one alcohol-affected child also produced others. Other findings indicated that the mothers of these children led "chaotic" lives and were frequently isolated from their communities.

May et al. (1983) compared their data on FAS prevalence among southwestern Indians with published data for Seattle (Streissguth et al. 1980b), Goteburg, Sweden (Olgard et al. 1979), and Roubaix, France (Dahaene et al. 1981). Although the various studies in this comparison did not use identical diagnostic criteria, the figures suggest that overall FAS prevalence among southwestern Indians is roughly similar to that seen elsewhere. Prevalence among the Navajo and Pueblo Indians falls within the worldwide estimate of 1 to 3 cases of FAS per 1,000 live births cited in the *Fifth Special Report*. However, the prevalence of FAS for the Plains tribes within the health units studied—nearly 1 FAS case in every 100 births—is the highest recorded to date (May et al. 1983).

The investigators postulated that these differences in FAS rates might be due to drinking patterns associated with the unique sociocultural dynamics of the three Indian cultures represented in the study population. Plains tribes allow more variation in drinking behavior for women, whereas the other two Indian cultures, especially the Pueblos, are likely to ostracize women who drink. The investigators suggested that ostracism might increase the severity and prolong the duration of abusive drinking, and that this not only may explain the high frequency of multiple alcohol-affected children borne by the same mothers but also the higher incidence of FAS among the Pueblos than among the Navajos (2 per 1,000 versus 1.4 per 1,000, respectively).

Not all investigators would agree with these interpretations, and some would argue that other factors, such as genetics, cultural variations in the types of beverages consumed, and other factors have not been convincingly ruled out as explanations for the observed differences. For example, a recent study (Kuzma and Sokol 1982), which is discussed later in this chapter, has provided evidence that both black race and the type of alcoholic beverage a woman consumes during pregnancy can significantly increase the risk of alcohol-related birth defects.

### Neuropsychological Studies of the Children of Alcoholic Mothers

Over the past 10 years it has become evident that children affected by prenatal alcohol exposure show great individual variations in the extent and severity of malformations and impairments. However, there have been no systematic studies of perceptual development in relation to the physical characteristics of alcohol-affected children.

A recent study in Sweden by Aronson et al. (1985) focused on developmental levels and profiles, perception, emotional stability, and other psychological features in

children of alcoholic mothers, with and without complete characteristics of FAS. Though the women were alcoholics, their consumption levels during pregnancy were unknown.

The majority of these children were found to have severely disturbed visual perception, whereas none of the matched control group had this problem. The children—11 boys and 10 girls ranging in age from 1.5 to 9 years—were paired with controls matched for sex, age, birth weight, gestational age, and living area. Traits associated with prenatal alcohol exposure (e.g., growth deficiency, impaired motor performance) with or without malformations were found in 10 cases, as described in a previous report by these investigators (Kyllerman et al. 1985).

In tests of intelligence, the controls were within the normal range for Swedish children, whereas the children of alcoholic mothers scored 15 to 19 IQ points lower. The 10 children with signs of FAS had significantly lower IQs and more pronounced perceptual delays than did alcohol-affected children who appeared physically normal. This correlation of lowered intelligence with FAS signs was said to be consistent with findings from other studies (Jones et al. 1974; Bierich et al. 1976; Streissguth et al. 1978). No significant IQ differences were found between children reared in foster homes and those reared in biological homes.

The alcohol-affected children also scored significantly lower in a number of other tests of development, including hearing and speech, eye-hand coordination, and practical reasoning. Difficulties were especially evident in these children in tasks demanding good eye-hand coordination, visual form perception, concept formation, and attention span.

Indicators of emotional instability were significantly more prevalent in the study group than in the controls. Hyperactivity, distractability, and short attention span were seen in 12 of the 21 children of alcoholic mothers, and perseveration (inability to shift readily from one activity to another) was seen in 6. These traits were not seen among controls.

### Electrophysiology of Infants of Alcoholic Mothers

Significant abnormalities in brain electrical phenomena were discovered in the infants of alcoholic mothers soon after FAS was first recognized. For example, significant abnormalities have been found in the electroencephalograms of babies born to alcoholic mothers, even in the absence of gross congenital anomalies associated with FAS (Havlicek et al. 1975), although the study did not clearly separate the effects of smoking from those of alcohol (most alcoholics are also smokers).

A new electroencephalographic study from the same institution (Chernick et al. 1983) has found evidence that alcohol has a specific effect on the fetal brain that is not linked to smoking. This study separated the effects of drinking and smoking by comparing electroencephalographic and morphometric data from infants of alcoholic mothers with the same kind of data from infants of smoking but nondrinking mothers.



Data were obtained prospectively from 70 infants born between 1975 and 1980. The infants were in four groups: those whose mothers drank more than 2 ounces of pure alcohol a day, a matched group of infants whose mothers were abstainers or drank less than an ounce of alcohol on any occasion, infants of smoking mothers who were non-drinkers, and a matched group of infants whose mothers neither smoked nor drank. Thus, the study included alcohol-exposed babies and tobacco-exposed babies, as well as control subjects for each group. The alcohol- and tobacco-exposed groups were matched with their respective controls as closely as possible for postconceptional age, sex, race, and socioeconomic status.

Electroencephalography at 39 weeks postconceptional age revealed much greater electrical activity in the brains of infants of the heavier drinking mothers than in their controls. The greatest differences were found during the rapid eye movement (REM) phases of sleep. In contrast, no electroencephalographic differences were seen between tobacco-exposed babies and their controls during any phase of sleep. Electroencephalograms from normal, alcohol-exposed, and tobacco-exposed infants are shown in figure 1.

The infants of alcoholic mothers showed abnormal behavior patterns—irritability, tremulousness, or jittery movements—and two of them had seizures that were judged to be the result of alcohol withdrawal. All infants of these mothers also had one or more complications after delivery. These included respiratory problems, small size for gestational age, and, in seven babies, FAS or congenital abnormalities including small head circumference. Infants of mothers who smoked had significantly lower birth weight and length but normal head circumference.

The investigators concluded that the electrical disturbances found in the brains of babies of heavier-drinking mothers are not related to concurrent maternal smoking, because no such disturbances were found in the babies of mothers who smoked but were not in the heavy-drinking category. The results also indicate that heavy maternal alcohol consumption affects the neonatal electroencephalogram even in the absence of any physical congenital anomalies. This suggested to the investigators that electroencephalography may be the most sensitive indicator of fetal alcohol toxicity. However, it is also possible that the electroencephalographic disturbances could be a sign of alcohol withdrawal in the infant rather than toxicity; also, the persistence and precise meaning of these electroencephalographic changes are not known.

## WHAT DETERMINES SUSCEPTIBILITY TO PRENATAL ALCOHOL DAMAGE?

Not all women who drink abusively during pregnancy deliver babies with FAS or alcohol-related birth defects. In fact, the frequency of FAS and alcohol-related birth defects is much lower than the frequency of abusive drinking among pregnant women. This has led to a hypothesis that other factors may modify the impact of alcohol on prenatal

development. The hypothesis is the subject of a recent article by Sokol et al. (1986).

In their epidemiological survey of more than 12,000 pregnancies in Cleveland, Ohio, the investigators have found 204 abusive drinkers (1.7 percent of the study population). Yet only 5 babies among the 204 offspring of these heavily drinking women had FAS, and no more than half of the 204 infants had any abnormality that could possibly be attributed to prenatal alcohol exposure (Sokol et al. 1980). A similar difference between rates of heavy prenatal alcohol exposure and adverse pregnancy outcome

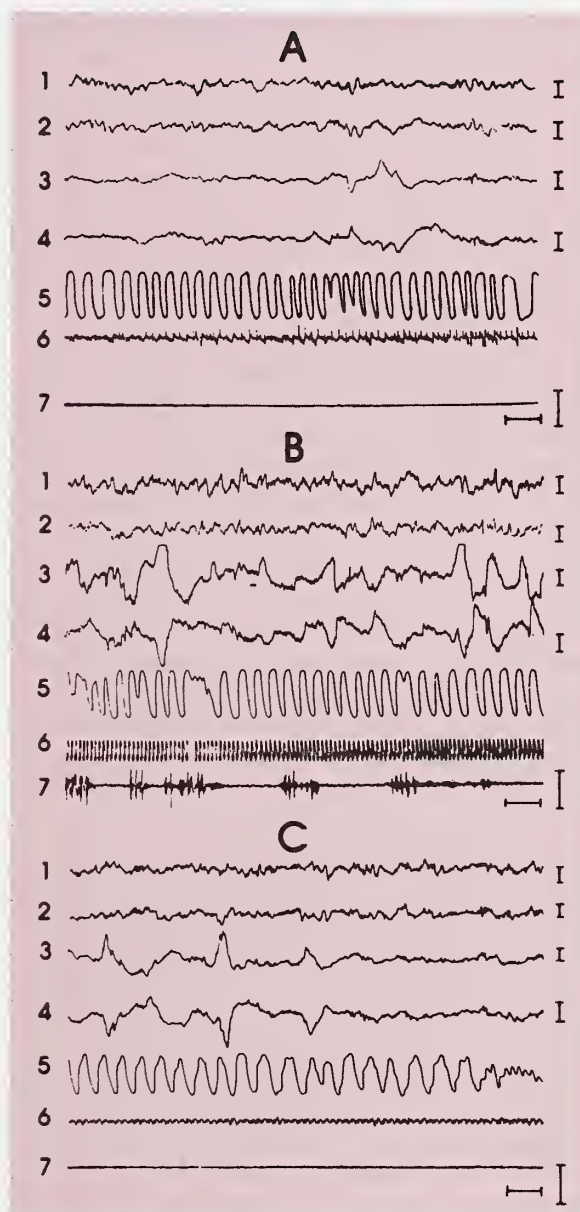


FIGURE 1. Polygraphic tracing in term infants (39 weeks' postconceptional age) during REM sleep. A, healthy control infant; B, infant of alcoholic mother; C, infant of smoking mother. 1, C<sub>3</sub>/A<sub>2</sub> electroencephalogram tracing; 2, C<sub>4</sub>/A<sub>1</sub> electroencephalogram tracing; 3, E<sub>1</sub>/A<sub>1</sub> electro-oculogram; 4, E<sub>2</sub>/A<sub>1</sub> electro-oculogram; 5, respiration; 6, electrocardiogram (II standard lead); 7, electromyogram from submental muscles. (Calibration: horizontal = 3 seconds; vertical = 100 mv.)

SOURCE: Chernick et al. 1983.



is also evident in data on infant neurobehavioral development from the Pregnancy and Health Study in Seattle. Among the 5 percent of pregnancies with the heaviest drinking, only 5 to 10 percent of the infants scored abnormally low on mental and psychomotor tests when tested at 8 months of age (Streissguth et al. 1980a).

Published literature on the question of what affects susceptibility is sparse, and there is a great need for more research in this area. A number of factors might explain why only some infants are damaged by heavy maternal drinking during pregnancy. For example, some embryos and fetuses may be genetically more susceptible to alcohol damage than others; variable maternal factors may have a protective effect; and fetal or embryonic damage may be enhanced by other risk factors that work synergistically with alcohol. Varying susceptibility may also be related to specific drinking patterns and peak blood alcohol levels attained, the effects of which have not yet been fully characterized. The investigators addressed the issue of susceptibility by examining two kinds of risk factors, those for intrauterine growth retardation and those for the full fetal alcohol syndrome.

As noted in the *Fifth Special Report*, low birth weight for gestational age is the most consistently reported effect of prenatal alcohol exposure. Sokol et al. (1986) examined the possibility that genetic factors might influence susceptibility to intrauterine growth retardation by reexamining data from 5,093 pregnancies that had been obtained in an early prospective study in Loma Linda, Calif. Of 44 potential determinants of birth weight that were examined, 10 were found to contribute significantly and independently to intrauterine growth retardation (Kuzma and Sokol 1982).

Level of beer consumption during pregnancy was one of the most significant contributing factors, indicating that type of beverage was important. An alcohol-related birth decrement of about 100 grams was seen only in the 176 pregnancies (3 percent) in which the mother consumed beer more than 20 days a month. This finding does not mean that consumption of wine, distilled spirits, or other alcoholic beverages during pregnancy is therefore risk free; numerous studies have shown that alcohol, as such and in whatever form it is consumed, poses a risk to proper fetal development and can be teratogenic. For some reason, however, heavy beer consumption during pregnancy appears to be associated with even greater risk.

Analysis of these 176 pregnancies in comparison with 149 other pregnancies that yielded infants with greater weight (more than 2,700 grams) indicated the following: the mothers of affected babies were more likely to be black (26 percent versus 7 percent); they were more likely to have weighed approximately 11 pounds less before pregnancy; and they were more likely to have gained an average of 5 fewer pounds during pregnancy. A further analysis of 2,233 pregnancies in which the mothers drank any amount of beer also revealed that growth retardation was associated with lower maternal weight before pregnancy, lower weight gain during pregnancy, ethnicity, and frequent beer drinking, as well as cigarette smoking. These associations were highly significant statistically.

Each of these factors appeared to operate independently of the others; that is, they were additive. It is possible, however, that abusive drinking might interact synergistically (more than additively) with other risks that were not measured in this study, for example, genetic predisposition. The investigators also note that since no factors were identified that interact negatively with alcohol to ameliorate its significant intrauterine growth retarding effect, abusive drinking should continue to be regarded as a risk in any pregnancy.

The examination of contributory risk factors for the full FAS used data obtained from the ongoing Cleveland Fetal Alcohol Study. The data base in this study consists of information gathered over a 33-month period on 8,331 consecutive pregnancies and includes patient identification, Michigan Alcoholism Screening Test (MAST) scores (a measure of history of alcohol problems), self-reported daily alcohol intake during the preceding 2 weeks, nutrition, other drug use, and medical and obstetric information.

From the approximately 11 percent of these women whose MAST scores indicated a prior history of alcohol problems, a group of 600 was recruited for study and matched for seven factors with 600 MAST-negative women. The newborn infants of all 1,200 women were then examined for alcohol-related birth defects by investigators who were unaware of the mothers' MAST scores and their drinking levels and patterns during the recently completed pregnancy.

Twenty-five cases of full FAS were identified (indicating an FAS rate of approximately 3 cases per 1,000 births in this population of 8,331 women). These 25 babies were matched with 50 non-FAS control infants to examine the issue of susceptibility to FAS. Statistical analysis of data from the two groups of infants and their parents revealed no differences in socioeconomic status, educational level, cigarette smoking, narcotic use, prepregnancy weight, nutrition, obstetric risk score, previous abortions, or father's weight. However, FAS was associated with increased maternal age, increased frequency in blacks, greater number of previous pregnancies, higher frequency of MAST positivity, greater proportion of drinking days and greater consumption of alcohol per drinking day, and a higher proportion of alcohol from beer.

Four variables accounted for 63.6 percent of the variance in FAS/non-FAS outcomes in this study: percentage of drinking days, MAST test scores, number of previous births, and race. Analysis revealed that if none of these four variables is present in heavy-drinking women, the probability of the infant having FAS is less than 2 percent. If all four are present (i.e., high percentage of drinking days, positive MAST score, high number of previous births, and black race), the probability of the baby being born with FAS rises to 85.2 percent, a more than 50-fold increase in probability.

The most striking finding, both in the growth retardation and the full FAS aspects of this study, is that race may increase susceptibility for FAS. The first study (the analysis of the Loma Linda data) found being black and frequently



drinking beer additively increase the chances of low birth weight for gestational age. The study in Cleveland found that black race considerably increases the risk for FAS to a level about seven times higher than for white infants who receive the same prenatal alcohol exposure. This finding is consistent with a recent report by Iosub et al. (1985), in which a comparison of the incidence of FAS in Hispanics and blacks revealed that single and multiple cases of FAS are more frequent in blacks.

Although these studies indicate that race may influence susceptibility to FAS, it is crucial to note that numerous studies around the world involving many ethnic and racial groups have shown that none are immune.

These results may have important implications for public health, clinical practice, and research, especially if they can be confirmed by others. From the standpoint of public health, they indicate the possibility of significant benefits from increased prevention efforts among disadvantaged black women, especially those with previous children.

Sokol et al. (1986) conclude that factors that may modify the susceptibility of the fetus to alcohol teratogenicity have not been adequately studied in the past, that much more research is needed in this area, and that studies of the impact of alcohol on human pregnancy outcome, particularly those related to neurobehavioral development, would do well to focus on factors that may additively or interactively modify the impact of alcohol on offspring.

## EFFECTS OF LOWER LEVELS OF DRINKING DURING PREGNANCY

Since 1973, hundreds of case reports have been published on children born with FAS, and it is now widely accepted by researchers that these severely dysmorphic children are born only to mothers who are chronic alcoholics and drink heavily during pregnancy. The prevailing view, however, is that the obvious developmental and behavioral aberrations of FAS represent only the most severe end of a continuum of fetal damage that can be produced by prenatal alcohol exposure, and that lower levels of maternal drinking may also have some measurable effect on the fetus.

Harmful effects on children at lower levels of maternal drinking during pregnancy can be expected to be more subtle, to occur less frequently, and to be more often neurobehavioral than physical. Their detection therefore requires longitudinal studies and statistical analysis of data from sizable populations of pregnant women and their offspring. In such studies a population of pregnant women is examined for level and pattern of drinking, as well as other lifestyle factors such as nicotine, caffeine, and drug intake, at one or more times during pregnancy. Followup studies of the children begin at birth and are repeated at intervals during the first few years of life. With a sufficiently large study population and use of appropriate statistical methods, it becomes possible to detect subtle behavioral deficits in the children, associate their type and extent with

maternal drinking levels during pregnancy, identify other risk factors, and estimate the incidence and prevalence of fetal alcohol effects in the general population.

One such study is a component of the Seattle Pregnancy and Health Study, now in its 10th year. In this longitudinal study, 1,529 predominantly white, married, middle-class women in prenatal care were interviewed during the 5th month of pregnancy about their alcohol, tobacco, and drug use and other lifestyle factors. The self-reported drinking levels in these women ranged from total abstinence to fairly heavy drinking. A cohort of about 500 children born to these mothers was then selected for followup studies over the first 7 years of life—at birth, at 8 and 18 months, and at 4 and 7 years of age. Followup studies on the children have now been completed through age 4.

These investigators have reported several neurological and behavioral effects in children whose mothers consumed alcohol either lightly, moderately, or fairly heavily during pregnancy, and on several measures the effects are proportional to the level of alcohol consumption during pregnancy. Neurological and behavioral effects were measurable from the first day of life at all three levels of maternal drinking (expressed as average daily intake of pure alcohol, the three levels of drinking were defined as follows: light drinking, 0.1 ounce or less per day; moderate drinking, 0.1 to 0.9 ounce per day; and heavy drinking, 1 ounce or more per day). The data so far do not suggest a threshold level of drinking below which there is no effect on the unborn child.

The findings from specific kinds of measurements, from birth through 4 years of age, are summarized in the following paragraphs. Some of the findings from earlier phases of the Seattle study have been presented in previous Special Reports on Alcohol and Health, but, because this is a continuing project, they are briefly summarized here so newer findings from the study can be seen in context.

### Habituation

The ability of a newborn infant to "tune out" and stop responding to a repeated extraneous stimulation is called habituation. Slowness in habituating is considered an indicator of delayed development of the central nervous system (CNS) (Lewis 1975). The Seattle study found a strong correlation between delayed habituation in newborns and the level of maternal drinking during pregnancy. That is, the more alcohol mothers consumed during pregnancy, the longer it took their babies to become habituated to a repeated stimulation and stop responding to it (Streissguth et al. 1983).

### Sucking Reflex

Two measurements of the sucking reflex were used in the Seattle study—the time required for an infant to begin sucking when presented with the appropriate stimulus and the strength of sucking once it commences. The Seattle study found that maternal drinking during pregnancy significantly prolongs the time it takes to begin sucking and significantly reduces the strength of sucking. Again, the



degree of impairment was proportional to the amount of alcohol the mothers had consumed (Martin et al. 1979).

### Other Newborn Behaviors

The infants of mothers who drank during pregnancy also showed increased body tremors, a greater tendency to turn the head to the left, and less vigorous bodily activity (Martin et al. 1979). The degree of these effects was proportional to the amount of drinking during pregnancy. Two additional differences, greater amount of time spent with the eyes open and greater hand-to-face activity, were seen only in the infants of heavier-drinking mothers.

### *Alcohol Effects at 4 Years*

The most recent findings from the Seattle longitudinal study show that alcohol-related neurological and behavioral effects have persisted in the children of the heavier-drinking mothers to at least 4 years of age (Streissguth et al. 1984b; Streissguth et al. 1984c). Furthermore, the more sensitive laboratory tests continue to show reduced attention and slower information processing even in 4-year-old children prenatally exposed to lower levels of alcohol. According to the authors, the 4-year-old children whose mothers were heavier drinkers during pregnancy show clear performance decrements in tests requiring vigilance and fast reaction. The investigators suggest that while the children of the heavier-drinking mothers may be clinically normal, their lowered vigilance and longer reaction time may represent minor alcohol-related CNS injury along the same continuum that includes the severe neurological and behavioral deficits that occur only at alcoholic levels of maternal consumption, that is, in FAS. Whether these lesser effects associated with lower levels of maternal drinking will persist and affect performance in school will not be known until the 7-year followup or beyond.

Streissguth et al. (1984b) advise caution in interpreting these findings. The study design is such that a variety of possible drinking patterns during pregnancy were grouped together in the same average daily consumption categories, and some of the drinking patterns within each average consumption level could be riskier than others (e.g., binge drinking, especially at critical periods of vulnerability, as opposed to a more steady pattern of drinking). Also, although neurological and behavioral deficits in infants and children were found associated with low to moderately heavy average daily alcohol consumption during pregnancy, the deficits were relatively small, and measurements in a large number of these children were required to achieve statistical significance.

Effects of lower levels of maternal drinking have also been examined in the Cleveland Fetal Alcohol Study (Ernhart et al. 1985). Fetal alcohol effects examined included specific physical anomalies, intrauterine growth retardation, and neurobehavioral deficits. This study examined 359 infants born to disadvantaged women, 176 of whom scored positive on the MAST and 183 of whom were MAST negative. Assessments of these newborns included a tally of alcohol-related physical anomalies; measurements

of weight, length, and head circumference; and neurobehavioral testing with standard procedures.

The number of physical anomalies was greater in the infants whose mothers had a history of alcohol abuse before pregnancy and was highest in those who were MAST positive and also had higher alcohol consumption levels during the first trimester. Persistent exposure to alcohol, at least in the first trimester, was the crucial factor in determining increased occurrence of neonatal anomalies.

Intrauterine growth deficiency was associated with being black, having smaller parents, and being female, but was independent of both earlier history of alcohol abuse in the mothers and their alcohol consumption during pregnancy. Ernhart et al. point out that though size effects are clearly a feature of FAS, they have not been consistently obtained in all studies of lower levels of alcohol exposure, perhaps because of "reasonable fluctuations of a small, but true, effect being assessed at or near threshold." In other words, growth-impairing effects of lower levels of maternal drinking may be real, but they are so small that they are difficult to measure reliably.

Neurobehavioral test scores in the Cleveland study were found to be unrelated to either MAST classification or amount of daily alcohol consumption during pregnancy. Also, scales relevant to central nervous system disturbances of FAS (hypotonia, hypertonia, tremulousness, irritability, and jitteriness) did not show any alcohol-related deficiencies. However, it may be that the amounts of alcohol consumed by the cohort of women in this study were not high enough to produce effects that could be detected by the neonatal tests. The Cleveland investigators suggest that "the critical tests of neuropsychological deficit in these children will be those related to intelligence and attention deficit in the preschool years" (Ernhart et al. 1985).

Adverse effects of "social" levels of drinking during pregnancy were also reported in a recent Canadian study (Gusella and Fried 1984) of 84 middle-to upper middle-class women and their babies. The study was part of the Ottawa Prenatal Prospective Study, which since 1978 has been examining the relationship between maternal lifestyles during pregnancy and infant development. Smoking was also assessed in the women because it is usually very strongly associated with alcohol consumption. During pregnancy the daily consumption of absolute alcohol by these women averaged 0.24 ounces, 0.20 ounces, and 0.18 ounces in the first, second, and third trimesters, respectively. During the first trimester, 33 percent of the women drank between 0.14 and 0.85 ounces a day, and 7 percent drank more than that amount. By the third trimester 39 percent drank between 0.14 and 0.85 ounces a day, and 1 percent consumed more than 0.85 ounces. Only one woman consumed more than an average of 1.5 ounces of absolute alcohol a day throughout pregnancy. Binge drinking was very infrequent in these women and therefore was not treated as a separate variable.

Developmental performance in the 84 offspring of these mothers was measured at 13 months of age using a standard test battery that includes scales for sensory perception;



memory; problem solving; vocalization; gross and fine motor movements; and attitude, interests, and temperament.

The tests suggested that "social" drinking during pregnancy was associated with lower scores on tests of spoken language and verbal comprehension in the children. Maternal smoking was found to be related to decreased motor performance as well as to decreased verbal comprehension. Although these results suggest that drinking at social levels or smoking during pregnancy might have adverse effects on the offspring, the clinical significance of the findings will not be known until long-term followup studies are made.

Some general observations can be made concerning longitudinal studies to determine the effects of nonalcoholic levels of maternal drinking on pregnancy outcome. First, in contrast to the relatively straightforward identification of FAS in the child of an alcoholic mother, such studies are difficult and complex, requiring long-term monitoring of women and their offspring to assess abnormalities that are often very subtle and the enrollment of large populations to achieve statistical significance. Second, even though the effects of social drinking during pregnancy may be small and not always easy to measure, they could constitute a significant public health issue in the aggregate because social drinking is so prevalent. Third, although effects measured in a population may be small at lower drinking levels, there may well be subgroups in the population who are more susceptible than average to fetal alcohol effects at social drinking levels. There is no way to identify such subgroups at present, but the ability to do so can come from long-range epidemiological studies such as those described here. It is important that such studies continue. Meanwhile, pending the clarification of susceptibility factors that such studies can provide, all women are well advised to avoid drinking during pregnancy.

## ALCOHOL AND CENTRAL NERVOUS SYSTEM DEVELOPMENT IN ANIMAL MODELS

Animal models play a very important role in the study of fetal alcohol effects because they allow those effects to be examined under carefully controlled conditions that are impossible to achieve with humans. Many of the physical features of FAS are reproducible in experimental animals, and this makes them valuable in studies aimed at understanding the mechanisms that produce the damage.

Damage to the developing CNS has long been recognized as one of the most serious consequences of heavy alcohol consumption during pregnancy. High vulnerability of the CNS to prenatal alcohol is suggested by the fact that nervous system effects can be measured even in the absence of outward physical abnormalities arising from in utero alcohol exposure. This is indicated both by epidemiological studies such as those cited above and by laboratory studies (Barnes and Walker 1981; West et al. 1981a, b). A

number of investigators have therefore been using animal models to examine the effects of prenatal ethanol exposure on specific structures within the CNS.

## A Nonhuman Primate Model of the Fetal Alcohol Syndrome

Studies with more common laboratory animals, such as rats and mice, continue to yield valuable information about the fetal alcohol syndrome that is relevant to the human condition, but direct extrapolation of findings to humans is not always easy. For example, findings from low and moderate alcohol dose studies in rodents cannot be cleanly extrapolated to humans because these animals metabolize alcohol much more rapidly than humans. This higher metabolic rate requires very high doses of alcohol to produce features of FAS. Furthermore, these animals lack complex cognitive functioning, which makes them less suitable for studies aimed at understanding neurobehavioral effects of prenatal alcohol exposure of the kind seen in humans. For these reasons, there is a need to develop primate models of FAS.

Preliminary studies show that nonhuman primates have great potential to provide answers to important questions about human FAS and other alcohol-induced fetal injury—for example, the alcohol dose required to produce a specific malformation, the risk of steady maternal drinking versus binge drinking at particular times during pregnancy, and the periods when the developing organism is most susceptible to damage from alcohol.

The developers of one model, which uses the Macaque monkey (Clarren and Bowden 1982, 1984; Bowden et al. 1983), report that intermittent alcohol administration to pregnant monkeys, an exposure pattern similar to binge drinking in humans, produced dose-dependent craniofacial and nervous system effects in offspring that were very similar to the human fetal alcohol syndrome, although none of the monkeys had all the features of FAS. Monkeys that had been exposed prenatally to moderate doses of alcohol appeared to have normal neurological and mental development. However, sensitive tests revealed significant neurochemical abnormalities in the moderate-dose monkeys, even though the outward appearance of the animals was normal. High prenatal alcohol exposure significantly impaired visual-auditory responses and motor development and caused profound mental retardation.

These preliminary findings indicate that primate models of the fetal alcohol syndrome are likely to be useful in clarifying the relationships between alcohol-related birth defects and the timing and amount of prenatal alcohol exposure. They are also likely to provide dose-response curves that are relevant to human pregnancy.

## Effects of Ethanol on Development of Specific Brain Structures

### *Hippocampus*

The hippocampus, a subcortical structure, has a relatively simple cellular organization, consisting predominantly of a single type of nerve cell. This together with evidence that



the hippocampus may be involved in learning (Lipp et al. 1984; Schwegler et al. 1981) makes the structure highly suitable as a model system for studying the teratogenic effects of alcohol on the brain. Studies in rodents have shown that prenatal alcohol exposure affects hippocampal development dramatically. Barnes and Walker (1981) found that ethanol exposure in the fetal rat during gestation days 10 to 21 significantly reduced the number of pyramidal cells, the predominant neurons in the hippocampus.

Other studies (West et al. 1981a, b; West and Hodges-Savola, 1982) provide evidence that exposure of developing rats to ethanol on gestation days 1 to 21 causes certain neurons (the mossy fibers, which bring nervous impulses from the dentate gyrus into the hippocampus) to terminate in a hippocampal area where they are not normally found and that this occurs in the absence of any external malformations in the animals. The pair-feeding experimental design of this research indicates that the abnormal termination of mossy fibers could not have been due solely to nutritional deficiencies associated with alcohol consumption by the pregnant rats. This abnormality persisted in the prenatally exposed rats until 9 months of age (the oldest animals tested). These results suggest that ethanol exposure in utero, during a period of brain development roughly equivalent to the first and second trimesters of human pregnancy, can cause permanent abnormalities in brain development.

Not all hippocampal structures are affected by prenatal alcohol exposure, however. Dewey and West (1985) recently reported that the terminations of neurons conveying impulses into the dentate gyrus (afferent neurons) in newborn rats were unaffected by heavy maternal alcohol exposure (35 percent of total calories) during the first 21 days of gestation. Further research is needed to explain why some neuronal systems in the hippocampal formation, such as the mossy fibers, are dramatically altered by prenatal alcohol exposure whereas others are not.

A more recent study (West and Hamre 1985) compared the effects on hippocampal mossy fiber development of short prenatal ethanol exposures in rats during periods corresponding to all three trimesters of human pregnancy. The greatest effects occurred in rat pups exposed to ethanol [at levels producing an average blood alcohol concentration (BAC) of 0.15 to 0.16 percent] during postpartum days 1 to 10, a period that corresponds to the third trimester of human pregnancy. Exposure during this period dramatically altered the microscopic organization of the mossy fiber terminal field. These findings suggest that alcohol exposure during a period equivalent to the third trimester of human pregnancy is more damaging to this brain structure than exposure during periods equivalent to the first or second trimesters.

Although the functional significance of mossy fiber alterations is not known, some evidence suggests that they might contribute to learning deficits; correlation has been demonstrated between displaced hippocampal mossy fiber terminations and impaired performance of rodents in a

learning task (two-way avoidance) (Schwegler et al. 1981; Lipp et al. 1984).

These animal studies showing hippocampal damage from alcohol in all three trimesters of pregnancy could have important implications for human pregnancy.

### *The Locus Coeruleus*

Other studies have examined the effects of ethanol exposure on the locus coeruleus, a midbrain structure rich in noradrenergic neurons (neurons that use noradrenalin, or norepinephrine, as a neurotransmitter). Several functions have been proposed for this structure including normal and abnormal neuronal processes associated with attention, memory, reinforcement, anxiety and fear, sleep and arousal, control of motor systems, dementia, depression, and schizophrenia (Mason 1981; Van Dongen 1981). This makes the locus coeruleus of interest to researchers on FAS, because several of the mental and behavioral abnormalities seen in FAS are consistent with alcohol-induced alterations in those functions.

Strahlendorf and Strahlendorf (1983) tested the hypothesis that the locus coeruleus may be an important site of CNS abnormalities caused by prenatal alcohol exposure. In electrophysiological experiments to determine whether ethanol can directly affect neurons of the locus coeruleus in adult rats, they found that ethanol administration, whether by intraperitoneal injection (1 to 2 g/kg) or by direct microiontophoretic application of dilute alcohol (0.3 M) to locus coeruleus neurons, markedly inhibited the spontaneous firing rate of individual neurons. The inhibition ranged from 6 percent to 100 percent and occurred in the absence of any detectable effects on the membranes of the locus coeruleus neurons.

Although these studies were done on adult rats, the great sensitivity of the locus coeruleus to alcohol, as well as the evidence that it may be the site of several CNS functions that are found impaired in association with maternal alcohol consumption, led the investigators to suggest that it could be a "strategic site" of ethanol's actions on the developing CNS. Clearly, however, this hypothesis needs to be tested in animals prenatally exposed to alcohol.

### *Effects of Alcohol on Axon Sprouting*

Neurons are cells with two kinds of extensions, dendrites and axons. The function of dendrites, which are short, highly branched filaments, is to receive nerve impulses from the axons of adjacent nerve cells or from sensory receptors. The axon conducts the nerve impulse either to the dendrites of other neurons or to receptors on muscles or glands. Thus, propagation of a nerve impulse is from the dendrites, through the cell body, then through the axon to the dendrites of adjacent neurons.

A nerve cell that dies cannot be replaced, but it is well established that an axon that has been severed from its cell body can be replaced if the cell body has not received lethal damage. This process, called axon sprouting, has recently been used as a tool to determine the effects of prenatal alcohol exposure on the regenerative ability of brain cells.



West et al. (1984) hypothesized that adult animals prenatally exposed to alcohol may have altered ability to regenerate severed axons. For their study they chose a hippocampal structure called the dentate gyrus, whose gross anatomical structure is so regular that the axons of millions of neurons extend in the same general direction from the same layer of tissue consisting largely of nerve cell bodies. Because the axons are so regularly arranged, they constitute a tissue layer of their own that can be surgically removed, thus simultaneously severing all the axons from their cell bodies. Axon sprouting in this system is readily assessed by periodically measuring the width of a regenerating tissue zone made up almost entirely of newly sprouted axons.

The investigators found that rats born to mothers that received alcohol as 35 percent of total calories during the first 21 days of gestation had a more robust axon sprouting response to dentate gyrus lesioning as adults than did control animals. This discovery is surprising (one might have expected impaired axon sprouting), and it may have serious implications. Although the physiological significance of the enhanced axon sprouting is unclear, the finding indicates that prenatal alcohol exposure causes brain abnormalities that can persist into adult life even in the absence of external physical abnormalities. The investigators further suggest that the functional significance of this persistent acceleration of axon sprouting might not become apparent until deleterious effects are unmasked by other factors later in life.

### Anatomical Studies of Alcohol-Exposed Mouse Embryos

A recent study (Sulik et al. 1984) examined the consequences on prenatal brain development of acute ethanol administration to pregnant mice on day 7 of gestation, a time corresponding to the third week of human pregnancy. This is the period of pregnancy in mice when the embryo is entering the gastrula stage, a phase of development in which the embryo takes the form of a "hollow ball" of cells. Gastrulation is an embryonic phase common to all animal species including man. Among the events occurring during gastrulation is the formation of a structure called the embryonic disc, which later differentiates to give rise to parts of the brain as well as features of the midface. Because brain damage and facial malformation are conspicuous features of FAS, the investigators reasoned that the time of formation of the embryonic disc could be a critical period for alcohol-induced embryonic damage leading to FAS, including its characteristic facial, cranial, and brain anomalies, as well as behavioral deficits and mental retardation.

The approach in this research was to administer alcohol intraperitoneally to mice on the seventh day of pregnancy to yield a peak blood alcohol concentration of about 0.2 percent (which would be judged major intoxication, though not lethal, in a human), then remove the embryos a few days later and compare them under the microscope with embryos removed from saline-injected controls. Ex-

amination of the embryos' head regions by scanning electron microscopy, a technique that yields photographic enlargements with an almost three-dimensional quality, as well as by conventional light microscopy of tissue sections, revealed a number of gross abnormalities in the brains and faces of alcohol-exposed mouse embryos.

The brain abnormalities included developmental deficiencies in the forebrain; abnormal development of the primordial hippocampus; malformations in the cerebrum, cerebellum, and a number of other brain structures; and overall reduction in brain size. Facial anomalies included reduced size of the nose, abnormally small separation of the nostrils, underdeveloped philtrum, abnormally shallow notch in the upper lip, and an exaggerated space between the nose and the upper lip. Nearly all these brain and facial anomalies are classic features of human FAS.

The significance of these findings is that they point to a period corresponding to the third week of human pregnancy as a time when the embryo may be especially vulnerable to teratogenic actions of alcohol that produce major features of FAS (although alcohol can damage the developing infant in various ways throughout gestation). If these findings can be extrapolated to human pregnancy, this alcohol-vulnerable stage of embryonic development would occur at a time when most pregnant women are still unaware of their pregnancy.

### Effects of Alcohol on the Developing Auditory System

A number of visual system anomalies are found in FAS, including ptosis, short palpebral fissures, strabismus (cross-eyes), hypertelorism (abnormal width between the eyes), microphthalmia, atrophy of the optic disc (the point where the optic nerve enters the retina), malformed retinal blood vessels, subnormal number of optic nerve axons, and blindness. In contrast to visual system studies, there has been little research on the effects of prenatal alcohol exposure on the auditory system, although there is good reason to think alcohol may affect that system. Low-set and malformed ears are common in FAS children; many of the individual visual, craniofacial, and other disorders found in FAS are often accompanied by impaired hearing when they arise from other causes during childhood; and alcoholism can cause hearing loss through neurological damage. Yet until recently neither children nor animals with FAS have been systematically examined for hearing deficits.

Recently, Church and Holloway (1984) published the results of their study of brain stem auditory evoked potential (BAEP) audiometry in rats prenatally exposed to alcohol. The aim of the study was to examine the effects of prenatal alcohol exposure on the maturation of the auditory system, both peripherally and in the brain stem, in newborn rats. The hypothesis was that prenatal alcohol exposure would impair postnatal development of the auditory pathway in young rats and that the impairment could be detected by BAEP audiometry.

The BAEP is a series of electrical waves that arise in the brain stem in response to high-frequency clicks, and its



various components reflect neurological events at several points along the auditory pathway. The waves are detected by attaching skin electrodes at specific points on the animal's head, amplifying the BAEP voltages, and recording the data on a moving chart. Thus, BAEP audiometry is a noninvasive and objective way to assess the development of the sense of hearing in an animal.

The investigators found that the delay (latency) between the click stimulus and the generation of the BAEP (a matter of milliseconds) grew progressively shorter with age both in rats prenatally exposed to alcohol and in controls, reflecting postnatal development of the auditory pathway in both groups. However, the progressive shortening of BAEP latency with age was considerably slower in rats whose mothers consumed alcohol as 40 percent of total calories during pregnancy. Their BAEP waves were also considerably weaker. Furthermore, the alcohol-exposed rats never overcame their hearing deficiency; although the differences between the groups were greatest early in postnatal development, the alcohol-exposed rats still had significantly longer BAEP latency at maturity. Thus, prenatal alcohol exposure impaired maturation of the sense of hearing in these animals and probably caused permanent hearing deficits. The fact that these animals eventually made up their early weight deficit but still lagged in hearing development at maturity suggests a toxic effect of ethanol on the developing auditory pathway.

## NEUROBEHAVIORAL EFFECTS OF PRENATAL ALCOHOL EXPOSURE IN ANIMAL MODELS

The need for better experimental control has also led to the development of animal models to investigate the neurobehavioral effects of prenatal alcohol exposure. As already noted in the discussion of human longitudinal studies, these effects can occur at lower levels of maternal drinking during pregnancy, even in the absence of physical anomalies. Children born to chronic alcoholic women often show mental retardation, hyperactivity, and perceptual-motor dysfunction, and children born to women who drink at lower levels tend to show more subtle neurobehavioral effects. A number of studies over the years have shown that rats and other laboratory animals exposed to alcohol prenatally exhibit similar neurobehavioral abnormalities.

Recent research reports using animal models of neurobehavioral impairment are discussed in this section. Significant new research in this area includes the effects of prenatal alcohol exposure on sucking behavior, learning, and sexual development. The findings from several of these studies appear highly relevant to prenatal alcohol exposure in humans.

### Nursing Behavior

As discussed in the section on the Effects of Lower Levels of Drinking During Pregnancy, human infants exposed to alcohol prenatally have been found to have

weak sucking responses and to take longer to begin sucking when presented with an appropriate stimulus (Martin et al. 1978, 1979). These effects have recently been replicated in rats by Chen et al. (1982).

The sucking response is one of the first responses displayed by infant rats, and its development follows a well-defined pattern (Hall et al. 1975, 1977; Blass et al. 1979; Blass and Teicher 1980). Until about 12 days of age, rat pups quickly attach to a nipple whether they are hungry or not. After the 12th day of life, however, hungry pups continue to attach rapidly but nondeprived pups attach progressively more slowly.

Because this pattern is so well-defined, Chen et al. (1982) reasoned that nipple attachment behavior in young rats might be ideal for detecting a developmental dysfunction resulting from prenatal alcohol exposure. Three pair-feeding experiments were performed with rat pups whose mothers consumed liquid diets containing 35 percent of calories as alcohol during pregnancy, in comparison with controls on the same liquid diet without alcohol and controls fed standard laboratory chow. In the first experiment, nondeprived pups were tested in groups of three (one from each of the three prenatal treatment groups) for nipple attachment to a chow-fed mother. The second experiment compared nipple attachment in the offspring of the three types of mothers (liquid diet with alcohol, liquid diet without alcohol, and laboratory chow). The third experiment tested the possibility that data from the other two experiments were the result of either social interaction effects from testing pups in groups of three or alcohol-induced changes in maternal behavior. In this experiment, rat pups from all three groups reared by their biological mothers, and a group of pups born to alcohol-fed mothers but transferred to surrogate chow-fed mothers at birth, were tested for nipple attachment, one at a time.

All three experiments found an age-related pattern of nipple attachment behavior in which attachment was fastest in pups 6 to 12 days old and slowed rapidly from 13 to 21 days of age. Prenatal alcohol exposure significantly slowed the speed of attachment in animals 3 to 9 days of age but not in the older animals. These effects of prenatal alcohol exposure occurred regardless of which dietary group the test mother belonged to, whether the pups were tested singly or in groups of three, and whether they were raised by their alcohol-fed biological mothers or by chow-fed surrogates. Thus, impaired sucking in the young rats was evidently caused by their prenatal alcohol exposure, and not by maternal variables in postnatal life.

Although the alcohol doses used in this study were high (35 percent of total calories as alcohol), these animal experiments complement the clinical observations of Martin et al. (1978, 1979) of impaired sucking in human infants born to mothers who consumed alcohol in "social" amounts during pregnancy. Sucking is vital to infant nutrition, and its impairment may play a role in retarded postnatal growth, which is one of the primary consequences of prenatal alcohol exposure (Streissguth et al. 1980b).



## Impairment of Conditioned Learning

When an animal is given an unpleasant stimulus along with one it would normally find pleasant, it soon learns to associate the two stimuli and thereafter avoids the pleasant one as well as the unpleasant one. The process, called aversive conditioning, is a kind of learning that results in passive avoidance of what would otherwise be sought.

This technique was recently used to measure the effects of prenatal alcohol exposure on the ability of newborn rats to learn taste aversion to saccharin, a substance they normally like. Riley et al. (1984) divided a group of pregnant rats into three feeding groups: those receiving a liquid diet containing alcohol as 35 percent of total calories, a control group fed the same liquid diet with the same number of calories but no alcohol, and another control group fed standard laboratory chow ad lib. At 5, 10, or 15 days of age, offspring from each group were infused with a saccharin solution through a tube attached to the oral cavity. After saccharin feeding, half the pups in each group were administered a noxious substance (lithium chloride) and the other half were given sodium chloride as a control. The animals were then tested at intervals for a conditioned aversion to the saccharin solution.

Taste aversion at 5 days was marginal in all groups. At 10 days of age, taste aversion to saccharin was learned equally well by all the prenatal treatment groups. Aversion was stronger at 15 days of age, but was substantially weaker in the rats that were prenatally exposed to alcohol than in the controls. Put another way, the alcohol-exposed rats were not very good at learning to associate saccharin with unpleasant sensations. The investigators conclude that taste aversion learning, a relatively easy procedure, appears to be sensitive to prenatal alcohol exposure, can be used to assess learning deficits in preweanling animals, and may be well suited for behavioral teratology screening.

Because other research has implicated the hippocampus in taste aversion learning (Gregg et al. 1978; Gemberling et al. 1980; Driscoll et al. 1982), the investigators suspect that the diminished ability of prenatally exposed rats to learn taste aversion may be due to impaired development of the hippocampus. As discussed earlier in this chapter, research by other investigators (Barnes and Walker 1981; West et al. 1981a, b; West and Hodges-Savola 1982; West and Hamre 1985) has shown that prenatal alcohol exposure produces gross abnormalities in the hippocampus and that impairment in other types of animal learning tasks is correlated with hippocampal damage (Schwegler et al. 1981; Lipp et al. 1984). Abnormal hippocampal development is further implicated as a possible cause of impaired aversion learning in the present experiments by the fact that impairment was not detectable in these animals until they were tested at 15 days of age. This is about the time when the dentate gyrus begins to develop rapidly in young rats (Altman and Das 1965). Thus, prenatal alcohol exposure in these experiments could have hindered this rapid development of the dentate gyrus, and this in turn might have reduced taste aversion learning.

## Effects on Sexual Development

Chronic alcohol exposure in adult men and women is known to cause disturbances in reproductive function (Van Thiel et al. 1975, 1977, 1978; Cicero et al. 1979; Cicero 1981), particularly in the levels of sex hormones. It is reasonable to think that it might cause similar disturbances in utero, especially because alcohol passes readily through the placenta and into the fetus.

Several animal studies have suggested that prenatal alcohol exposure does indeed produce effects on the developing endocrine system and furthermore that these effects may persist into adult life. There have been reports of altered levels of gonadal hormones and corticosterone (Kakihana et al. 1980; Rose et al. 1981) and altered sexual development (Boggan et al. 1979; Chen and Smith 1979) in the offspring of animals fed alcohol during gestation.

Recently, McGivern et al. (1984) reported that prenatal alcohol exposure altered preference for saccharin in male and female rats. Female rats normally have a stronger preference for saccharin solutions than males, a behavior that is said to be "sexually dimorphic." However, prenatal alcohol exposure in male and female rats altered this behavior, making the males more female-like and the females more male-like in their preference for saccharin. These investigators speculate that the "feminized" behavior in the males may be caused by decreased testosterone levels during fetal life and that the "masculinized" behavior in the females may be caused by increased secretion of adrenal steroid hormones. If this research can be confirmed, it would support a hypothesis that endocrine imbalance from prenatal alcohol exposure can have long-term consequences (Anderson 1981).

A hypothesis of endocrine imbalance is also suggested by a recent report by Barron and Riley (1985) that prenatal exposure to alcohol significantly reduces maternal behavior in adult and juvenile rats. Normally, maternal behavior arises spontaneously in virgin rats repeatedly exposed to young pups. After about a week of exposure to pups, both males and females will groom them, retrieve them if they stray from the nest, and hover over them in a nursing posture. The behavior is not under hormonal control in the adults, but previous studies have revealed that prenatal and postnatal hormonal manipulations can significantly affect its subsequent development (Rosenblatt et al. 1979). This suggested to Barron and Riley that alcohol's known ability to disturb the developing endocrine system in utero might cause interference with the subsequent development of maternal behavior.

In studies to test this hypothesis, adult females that had been exposed to alcohol prenatally (alcohol comprising 35 percent of total calories in the diets of their mothers) showed significant deficits in maternal behavior in comparison with controls. They were about half as fast as controls in retrieving strayed pups, spent about half as much time hovering near or over them as the control rats, and had a greater tendency to cannibalize the young (a behavior more typical of adult male rats). Adult male rats given the same prenatal exposure to alcohol failed to show these



effects. However, when the tests were performed with juvenile rats, both sexes showed impairment of spontaneous maternal behavior. Significantly, the impaired maternal behavior dissipated with age in the males but not in the females.

A recent study has also demonstrated that prenatal alcohol exposure has adverse effects on the sexual behavior of adult male rats (Parker et al. 1984). Compared to controls, adult males whose mothers were fed a diet containing 36 percent of calories as alcohol throughout pregnancy had significantly reduced testicular development and lower plasma testosterone levels at maturity. Also, when paired with females, the males showed significantly lowered sexual motivation and performance. Because of these findings, Parker et al. suggest that male children of alcoholic mothers, particularly those with FAS, be observed carefully for evidence of psychosocial dysfunctions indicating abnormal sexual maturation.

## STUDIES OF THE MECHANISMS OF FETAL ALCOHOL DAMAGE

The actual mechanisms of alcohol-induced birth defects are still unknown, although numerous studies show that alcohol and acetaldehyde, its first metabolite, are directly toxic to the embryo and that alcohol can interfere with systems involved in the maintenance of pregnancy. The likelihood is that several mechanisms are involved, and that different mechanisms may underlie alcohol-induced retardation of fetal growth and alcohol-induced congenital anomalies. Among the possibilities being examined, in addition to direct embryotoxic and fetotoxic effects of alcohol and its metabolites, are fetal malnutrition and mineral deficiencies arising from maternal alcoholism, impaired delivery of oxygen to the fetus, derangements of deoxyribonucleic acid (DNA) and ribonucleic acid (RNA) metabolism, and impaired incorporation of amino acids into protein molecules (see review by Abel 1983). One of the newest areas of research on alcohol teratogenicity is the prostaglandin system.

### The Possible Role of Prostaglandins in Fetal Alcohol Damage

An intriguing and potentially very important hypothesis arising from recent research is that prostaglandins may be involved in some way in the mechanism of alcohol-induced birth defects. Prostaglandins are a family of complex derivatives of polyunsaturated fatty acids whose normal function is to modulate certain cellular functions in the body. These compounds are biologically potent and have a hormonelike action in that they can affect functions in tissues distant from the site of their production. Different members of the group can produce different effects, such as stimulation of smooth muscle, lowering of blood pressure, and antagonism to the action of certain hormones.

Because the prostaglandins are so potent, it is important that their concentrations be maintained at the proper physiological level. Excess production of certain prostaglandins is involved in pain and inflammation, for example, and it is significant that one of the most effective drugs for

treating those conditions—*aspirin*—turns out to be an inhibitor of prostaglandin synthetase, a key enzyme in the synthesis of prostaglandins (Vane 1978).

It has been proposed that prostaglandins play a role in the etiology of alcohol-induced birth defects (Pennington et al. 1983), and there is evidence from animal studies that aspirin and other prostaglandin synthetase inhibitors can antagonize some prostaglandin-mediated effects of alcohol. These include alcohol-induced sleep (George and Collins 1979), hypothermia (lowered body temperature) (George et al. 1983), and increased activity (Ritz et al. 1981) in adult mice.

These previous reports led Randall and Anton (1984) to hypothesize that aspirin might also antagonize the teratogenic actions of alcohol. To test the hypothesis, the investigators randomly assigned 30 pregnant mice to four treatment groups: aspirin and alcohol, buffer and alcohol, aspirin and saline, and buffer and saline. Aspirin solution (150 mg/kg), buffer, or saline were injected subcutaneously on the 10th day of gestation. An hour later each mouse received an intragastric injection of either alcohol solution (5.8 g/kg) or a saline solution (containing sugar to replace the alcohol calories).

This single acute dose of alcohol given on the 10th day of mouse pregnancy caused prenatal mortality, birth defects, and decreased fetal weight, confirming similar findings in mice by other investigators. The most dramatic finding, however, was that there were less than half as many malformations in the fetuses of mice that had received aspirin before alcohol compared to controls that had been exposed to alcohol only: 25 percent versus 54 percent. Also, aspirin pretreatment virtually eliminated alcohol-induced fetal mortality, although it had no significant protective effect against low fetal weight caused by prenatal alcohol exposure. These findings, and the controlled nature of the experiments, led the investigators to conclude that it was aspirin itself, and not other possible associated factors, that provided significant protection to the mice.

According to the investigators, this is one of the first reports of antagonism of alcohol teratogenesis by pharmacological intervention. It is important to emphasize, however, that these findings do not mean that pregnant women may now drink safely as long as they dose up with aspirin beforehand. These studies were done on a different species, the dose of aspirin was very high, and it was injected. Furthermore, aspirin did not prevent birth defects in these animals; it only reduced their frequency to a level that was still very high. Finally, aspirin is not a risk-free drug, and the combination of aspirin and alcohol carries an increased risk of gastric bleeding, as discussed in previous Special Reports to Congress.

The real significance of this study is that it opens up potentially fruitful new areas of research to understand the mechanisms behind alcohol-caused birth defects. Although there is good reason to suspect the involvement of prostaglandins in alcohol teratogenesis, further work is needed to demonstrate conclusively that aspirin prevents alcohol-related birth defects by interfering with prostaglandins.



The investigators point out that other possible actions of aspirin besides prostaglandin inhibition, such as alterations in alcohol metabolism, might also explain their results.

## CONCLUSION

From this sampling of major currents in the field of fetal alcohol research it is evident that progress is being made in understanding one of the major known causes of birth defects. There is still much to be learned, however, especially about the more subtle neurobehavioral effects of social drinking, the contributory risk factors for FAS, and the fundamental mechanisms by which alcohol damages the developing organism.

## SUMMARY

Effects of prenatal alcohol exposure on infants are measurable over a broad range of maternal drinking levels, including even "social" drinking. The best advice for pregnant women continues to be to abstain from alcohol. There is still no evidence to establish a level of alcohol consumption free of any potential risk to the fetus.

A 10-year followup study of adolescents who were born with the fetal alcohol syndrome indicates that its effects are permanent. The correlation between severity of mental retardation and severity of physical deformity and growth deficiency has persisted into adolescence. Although good quality of home life is associated with improved social and emotional development in these children, it does not ameliorate the severe handicaps caused by heavy prenatal alcohol exposure.

A neuropsychological study of children of alcoholic mothers, including some children with FAS, found IQ scores 10 to 19 points lower than controls, as well as retarded development of hearing and speech, eye-hand coordination, visual form perception, concept formation, and practical reasoning. Emotional instability, hyperactivity, distractability, short attention span, and perseveration were also significantly more prevalent in the children of alcoholic mothers.

The reported prevalence of FAS varies according to location and the population under study, but a commonly accepted general estimate is 1 to 3 cases per 1,000 live births. Epidemiological research indicates high prevalence of FAS in some American Indian populations. The prevalence of FAS varied among the Indian cultures studied, with certain groups of the Plains culture showing the highest prevalence yet recorded (9.8 FAS infants per 1,000 births), followed by the Pueblo (2 cases per 1,000 births) and the Navajo (1.4 cases per 1,000 births). These differences may be attributed to sociocultural factors affecting severity of alcoholism, but general maternal health, nutritional factors, genetics, and beverage preferences do not appear to have been convincingly ruled out.

Although these studies, and numerous others, have linked maternal alcoholism with birth defects, only a small percentage of women who drink at alcoholic levels during pregnancy give birth to babies with the fetal alcohol syndrome. This suggests that other factors modify the

impact of alcohol on prenatal development. A recent epidemiological study of more than 8,000 women indicates that the most significant contributing factors to prenatal alcohol damage include persistent drinking during pregnancy among women with chronic alcohol problems, previous history of alcohol problems in the mother, increased parity (i.e., number of previous deliveries), and race. These four contributing risk factors accounted for nearly two-thirds of the variance in FAS/non-FAS outcomes. If all four of these additional factors were present, the probability of the baby being born with the fetal alcohol syndrome was 50 times higher than if none was present. These findings indicate that studies of the impact of alcohol on human pregnancy outcome would do well to focus on factors that may modify the impact of alcohol on offspring.

Although the full fetal alcohol syndrome is now more clearly linked to maternal alcoholism during pregnancy, lesser alcohol-related effects are observed at more moderate levels of consumption. For example, longitudinal studies in Seattle of the children of women who drank at low to moderate levels during pregnancy (i.e., "social" drinkers) reveal a higher incidence of subtle alcohol-related neurological and behavioral effects that have persisted from the time of birth to at least age 4. The magnitude of these effects on several measures was related to the amount of drinking during pregnancy. These neurobehavioral effects at lower drinking levels were not replicated in a longitudinal study in Cleveland, perhaps because these effects in the population studied were too subtle to be detected. But adverse behavioral effects from "social" drinking during pregnancy were reported from a recent study in Canada.

Animal models of FAS continue to provide information relevant to humans. Studies with animals have allowed detection and analysis of a number of effects of prenatal alcohol on the developing central nervous system and related structures. Prenatal alcohol exposure reduces the number of neurons in the hippocampus of the brain and causes certain hippocampal neurons to terminate in incorrect locations. The hippocampus is involved in aspects of learning, a function that is conspicuously impaired in FAS. Alcohol exposure can also profoundly affect the functioning of the locus coeruleus, a brain structure believed to be the seat of many behavioral functions that are known to be abnormal in FAS. The extreme sensitivity of the locus coeruleus to alcohol suggests that this structure could be a strategic site of alcohol's actions on the developing central nervous system. Also, axon sprouting, the neuronal process whereby new axons are regenerated to replace those that have been severed from their cell bodies, is significantly enhanced by prenatal alcohol exposure, even after animals have reached the adult stage. The physiological significance of this enhancement is unknown, but the implications could be serious because the altered axon sprouting persists into adult life and occurs even in the absence of external physical abnormalities.

Prenatal alcohol exposure has long been known to cause visual system anomalies in humans, but little attention has been paid to alcohol's effects on the developing auditory



system. New findings from animal studies indicate that alcohol interferes with the development of the sense of hearing through adverse effects on the developing auditory pathway.

Studies of alcohol-exposed mouse embryos by scanning electron microscopy implicate the gastrulation stage of embryonic development as a time of particular vulnerability to alcohol toxicity leading to craniofacial and brain anomalies characteristic of FAS in humans. Gastrulation in humans occurs in the third week of pregnancy, a time when most women are unaware that they are pregnant.

Animal studies have also revealed a number of neurobehavioral effects from prenatal alcohol exposure that complement findings in humans; for example, such studies have demonstrated that alcohol exposure in utero interferes with sucking behavior and learning ability. There is also evidence suggesting that prenatal alcohol exposure in animals produces changes in hormonal systems involved in the development of maternal behavior in adult females and sexual performance in adult males.

In a study to examine the role of prostaglandins in alcohol-induced malformations, aspirin was found to have a strong protective effect against both malformation and prenatal mortality in mice. Although the mechanism is unknown, evidence suggests that the protective effect may be due to aspirin's known ability to interfere with prostaglandin synthesis. The discovery points to the prostaglandin system as a potentially fruitful area of research to understand the mechanisms underlying alcohol-induced birth defects.

Collectively, the research reports described in this chapter demonstrate that significant progress is being made in understanding the effects of alcohol on the developing organism but that many unanswered questions remain.

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# Prevention and Intervention

The goal of both prevention and intervention efforts is to reduce the incidence of alcohol-related problems. Prevention measures are addressed to large populations, including those who may not yet drink. Intervention strategies are targeted to more discrete groups or individuals, such as those who consume alcoholic beverages either heavily, frequently, or under conditions that endanger health, life, or property; the goal is to help these people obtain early treatment or so modify their behavior as to eliminate or minimize the risk. Interpretation and emphasis often determine whether a particular measure is defined as prevention or as intervention.

This chapter discusses two major categories of prevention measures: (1) education and communication and (2) laws and regulations. It also reviews four types of intervention efforts: (1) training of primary health care providers, (2) programs for children at risk, (3) employee assistance programs, and (4) server intervention strategies.

## PREVENTION: EDUCATION AND COMMUNICATION

### Public Education

Public education includes strategies and programs designed to build awareness, improve knowledge, change attitudes, and modify behavior of the general public, thereby reducing alcohol-related problems. This discussion covers mass media campaigns, community-based programs, and education of parents.

#### *Mass Media Campaigns*

Mass media campaigns are employed to educate the public or specific target populations about specific health risks and ways to modify behaviors that contribute to such risks.

Existing research indicates that mass media campaigns by themselves do not change health behavior but can be effective in changing awareness, knowledge, and attitudes and can create a context in which other strategies to change behavior can succeed (Rootman 1985).

Mass media campaigns about drinking and driving have increased public knowledge. Two anti-drinking-and-driving campaigns conducted in Canada used both broadcast and print media (Pierce et al. 1975; Vingilis et al. 1979). One campaign combined increased law enforcement with media (Vingilis et al. 1979) while the other—a 30-day campaign—used only the media. Neither campaign employed community organization or involvement. The results of both campaigns indicate knowledge gains. The month-long campaign that used only the media produced several small positive changes in self-reported behavior (Pierce et al. 1975).

Mass media campaigns can be substantially improved by using principles from the advertising and marketing industry. Techniques such as defining specific audiences and targeting messages may increase the effectiveness of public

communication campaigns, but these techniques have limited efficacy for changing health-related behavior (McGuire 1984, 1985).

Mass media campaigns may ultimately serve to reinforce existing attitudes and social norms (Roberts and Maccoby 1985). Campaigns can also be effective when combined with other prevention strategies, such as increased enforcement of drinking-and-driving laws (Flay and Sobel 1983), publication and diffusion of materials, workshops, committees, community forums, and other community efforts (Rootman 1985), and integration into focused health promotion programs (Perry and Jessor 1985).

Flay and Sobel (1983) conclude that the most appropriate role for mass media campaigns in preventing alcohol and drug abuse is to increase the dissemination technologies found to be effective in other settings such as classrooms and clinics. They found that the chief weaknesses in media campaigns are a heavy reliance on information and fear messages, lack of targeted messages to identifiable audience segments, and very limited dissemination of the messages and materials.

### *Community-Based Programs*

Community-based programs are initiatives that use a defined community as the setting for alcohol prevention programming. Currently, few definitive studies provide knowledge as to the efficacy of the community as a site for alcohol abuse prevention programs, but there are experimental demonstration health promotion programs, the goal of which is to reduce the risk factors associated with cardiovascular disease such as a high-cholesterol diet, lack of exercise, and smoking. In the Stanford Heart Disease Prevention Project, three towns in California served as the test population; two towns were used as the experimental group receiving treatments, and one town was used as the control group receiving no treatment. The treatment for one of the experimental towns consisted only of health education messages via the mass media. In the second town, the general population received health messages and a randomly selected group of high-risk people received a 14-week intensive education and training program plus in-home counseling.

After the first, second, and third years, medical examinations were conducted. The overall cardiovascular risk for both towns that had received the education campaign had been reduced by 18 percent. In the control town, which had received no education campaign, overall cardiovascular risk increased by 6 percent. During year 3, there was slight regression in the experimental town that had received only the mass media education campaign. The positive health effects were longer lasting in the town receiving the mass media education campaign along with the intensive instruction and in-home counseling (Farquhar et al. 1981). While this landmark study is now being replicated in a number of demonstration project sites throughout the United States, it has to date not been extensively applied to alcohol problems.

The sustained behavior change resulting from the mass media campaign along with face-to-face instruction may

provide direction for future community-based programming in alcohol abuse prevention.

In one 3-year program in California that attempted to replicate the Stanford Project, researchers compared the results in three communities that were exposed to mass media messages and to educational and organizational strategies based in the communities themselves. After the programs had been administered, an evaluation of knowledge, attitudes, and behavior indicated somewhat greater knowledge about drinking but no significant change in attitude or behavior (Wallack and Barrows 1981).

### *Education of Parents*

Many experts believe that getting parents involved in alcohol prevention programming is an effective strategy. A review of 127 evaluations of drug abuse prevention programs indicates that programs that use peers and parents are more effective than those that use only teachers (Schaps et al. 1980). Prevention programs are seeking to train parents to help shape positive health behaviors in their children (Flay and Sobel 1983). The research to provide a scientific basis for parental involvement in alcohol abuse prevention is limited (Bry 1983). One study that took place over a 4-year period used a quasi-experimental design. The parents were given a 20-hour study program based on parent effectiveness training. The results indicated short-term improvements in the parenting skills as well as in the children's perceptions of their families. The children of the participants also increased their alcohol use, perhaps because most of the parents in the study used alcohol (Bry 1983).

There is a substantial amount of research literature on evaluations of parent education programs that were not designed specifically to prevent alcohol or drug abuse (Dembo et al. 1985). These programs are based on social learning theory, parent effectiveness training, and Adlerian approaches, and are intended to help parents understand their children's motivations and behavior. These studies indicate positive changes in parental attitudes but no change in the behavior of the participants' children (Dembo et al. 1985).

These parent-training programs have largely targeted white middle-class parents. One study (Alvy and Harrison 1982) tested the reaction of black parents to the ideological principles and offerings of three of the more popular parent-training programs (Gordon 1970, 1976; Aitchison 1976; Dinkmeyer and McKay 1976a, b; Eimers and Aitchison 1977).

A group of black Head Start parents were interviewed to discern their child-rearing practices. A group of white middle-income parents were interviewed and compared with the black parents on the major conceptual components of these three programs. Components of the programs were found to have wide appeal among white middle-class parents, but many of the components were rejected by black lower-income parents. Black parents in the study appeared to be less permissive; they viewed obedience and respect as the most desired outcomes of discipline (Alvy and Harrison 1982). This finding has merit



in indicating the necessity for tailoring parent education programs to address cultural differences in child-rearing practices.

### School-Based Programs

School prevention programs to reduce the incidence of alcohol use can be divided into three models. The models are designed to (1) increase knowledge and change attitudes, (2) teach values and decisionmaking skills, and (3) develop social competency skills. The research on these models is limited and there are no consistent findings about the efficacy of any of the three in preventing alcohol abuse by elementary or secondary students. Educational programs in schools have not been able to prevent alcohol abuse or to delay alcohol experimentation by elementary school youngsters. Many of these programs increase alcohol and drug knowledge, but few are known to influence attitudes and behavior about drug use or alcohol misuse. In general, the evaluation literature on these programs tends to be weak methodologically, and no definitive conclusions can be drawn.

#### *Elementary and Secondary Schools*

A review of the evaluations of 127 primary drug abuse prevention programs for young people measured their effects on use of drugs, intentions to use drugs, and attitudes toward the use of drugs (Schaps et al. 1980). (Alcohol was one of the drugs included in 61 of the programs.) Ten types of prevention strategies were identified and studied: information, persuasion, affective skill building, affective experience, counseling, tutoring/teaching, peer group activity, family activity, program development, and other alternatives. Programs delivered by peers or by parents were found to have had more positive outcomes than others. Of 10 exemplary programs, 1 (an informational program) was assessed as being somewhat counterproductive; the other 9, which consisted of affective or peer group interventions, were relatively successful (Schaps et al. 1980).

Other reviews of evaluation studies of alcohol or drug education (Goodstadt 1980; Hanson 1980; Kinder et al. 1980, all cited in Braucht and Braucht 1984) found the outcomes to be inconsistent. The reviewers also questioned the basis of the theoretical connection between changes in knowledge, attitude, and behavior. Braucht and Braucht (1984) suggest that educational programs and the methods used to evaluate their effectiveness would be more successful if they were created with this question in mind: What kinds of educational strategies have what kinds of effects on what kinds of young people?

A recent alcohol education evaluation study employing a pretest-posttest comparison group design found that students who had been exposed to a "facts curriculum" had reported a lower alcohol consumption rate—a result that was sustained at a 6-month followup. In the same study, members of an experimental group that was exposed to a facts curriculum to which values clarification and decision-making had been added showed posttest consumption rates higher than the rates for the group exposed to facts only.

This finding suggests that values clarification and decision-making programs serve to undermine the effectiveness of a knowledge/attitudes curriculum (Schlegal et al. 1984).

Other studies using strong research designs have had mixed findings. Programs using the social influences approach have yielded few answers. A 20-session program, the findings of which indicated a reduction in alcohol, cigarette, and marijuana use when the program was taught by trained high school students (Botvin et al. 1984), failed to produce the same or similar results when taught by classroom teachers.

A four-session curriculum for fifth- and sixth-grade students focusing on the social influences to drink failed to produce any effect on students' expressed desire to consume alcoholic beverages in the future, even though the youngsters in the program possessed the necessary refusal skills (saying no) at the beginning of the course (Shope and Dielman 1985). This finding raises questions about the efficacy of teaching refusal skills as a strategy to prevent alcohol abuse.

The use of alcohol, the use of other drugs, and the use of tobacco by young people have been found to be associated with one another and with other behaviors related to health, such as precocious sexual activity and delinquency (Botvin 1983). Smoking prevention programs using social influence approaches are of interest, then, not only for their effects on smoking but also for their possible application to the prevention of alcohol-related problems and drinking.

Flay's (1985) review of 17 school-based smoking prevention studies found that evaluations of approaches based on social influence contained significant methodological problems, including attrition by participants and inadequate reporting of data. Such approaches focus on "(a) teaching students about the social influences to smoke, (b) providing them with behavioral skills with which to resist those influences, and (c) correcting their perception of social norms" (Flay 1985, p. 67).

The most recent studies reviewed by Flay (1985) support the hypothesis that the social influence approach helps prevent the onset of smoking, but much work still is needed to investigate the internal validity of the research and, significantly, its generalizability to the primary prevention of alcohol abuse and alcohol-related problems. Whether such strategies as peer leadership and psychological "inoculation" may be used effectively to prevent alcohol abuse remains unknown (McAlister 1983).

The use of affective programs and peer leaders has been considered an appropriate strategy in prevention studies with young people (Botvin and Eng 1982; Telch et al. 1982; Botvin et al. 1984; Rootman 1985). A 12-session smoking prevention program was tested on more than 400 seventh graders (Botvin and Eng 1982). The program emphasized acquiring basic life skills and improving personal competence, especially coping with social influences to smoke. The multicomponent program's peer leaders were confident, nonsmoking high school students. Comparisons were made between students who received the peer intervention and those who did not, in terms of smoking status and



several variables of knowledge and psychological status believed to be related to the onset of smoking. Those seventh graders who participated in the peer leadership program exhibited a lower rate of beginning smoking, as well as differences on knowledge variables and psychological measures.

In another study, also involving seventh graders, a broad-based program designed to prevent alcohol misuse targeted the major cognitive, attitudinal, social, and personality factors believed to lead to early alcohol abuse (Borvin et al. 1984). Material was included on decisionmaking, ways to cope with anxiety, general social skills, and assertiveness, including methods of resisting peer pressure to drink. The program included information on the short- and long-term consequences of alcohol abuse. A significantly greater portion of the children who were assigned to the program reported less frequent drinking, less alcohol consumed when they drank, and fewer episodes of drunkenness than did the children in the control group. The program, however, had no impact on preventing or delaying early use of alcohol (Borvin et al. 1984).

### *College Campuses*

A review of 14 evaluations of alcohol education programs on college campuses shows promise. The programs employed strong evaluation designs using both control and treatment groups for comparison (Goodstadt and Caleekal-John 1984). All the programs used a knowledge/attitudes model, and three included a values/decisionmaking component. Participants in five of the programs reported fewer alcohol problems at posttest followup (Rozelle and Gonzalez 1979; Waring 1980; Robinson 1981). The "unsuccessful" programs ranged from 2 to 20 hours; the positive effects of the "unsuccessful" program had disappeared after 4 months. Programs that ranged from 20 to 36 hours were "successful"—meaning that the behavior change lasted substantially longer. Three of the successful programs also included field experiences<sup>1</sup> (Goodstadt and Caleekal-John 1984). Two other studies found that field experiences seem to contribute to program efficacy. In these two studies, two similar prevention programs were compared. One included field experiences while one included only classroom instruction. The program with the field experience was found to have a positive effect on participants (Dennison 1977; Dennison and Prevet 1980).

Two other evaluations of college programs looked at the use of media, discussion groups, and experimental workshops as components in a college prevention program (Mills et al. 1983; Kraft 1984). Efforts were made to modify campus regulations and practices regarding alcohol use (Kraft 1984). These efforts may be comparable to field experiences in the other college studies just described. However, the findings revealed evidence of change in

knowledge and attitude but no evidence of change in behavior (Kraft 1984).

Moskowitz (in press) challenges the positive picture that Goodstadt and Caleekal-John (1984) present on the effectiveness of college programs. He points out that an alternative explanation for the "success" of the programs is the use of nonequivalent control groups. All the students involved as the treatment population were volunteers who selected a 20- to 36-hour course about alcohol use. They very likely were highly motivated to change their lifestyles. Any reported effects may be due not to the programs but to bias in the selection of the participants. Future research must control for this bias before one can conclude that there is an empirical basis for the efficacy of these programs (Moskowitz 1986).

### *Advertising of Alcoholic Beverages*

The impact of alcohol advertising on alcohol consumption and alcohol-related problems remains controversial.

#### *Impact on Alcohol Consumption and Problems*

A recent review of the literature concludes that (1) marginal changes in expenditures for alcohol advertising, within the usual range, have little or no effect on total alcohol consumption, and (2) existing studies shed "virtually no light" on the relationship between advertising and alcohol abuse (Federal Trade Commission 1985).

The studies reviewed included econometric analyses (the application of statistical methods to the study of economic data and problems) of the impact of changes in expenditures for advertising (for alcohol, tobacco, and other products), studies of the association between self-reported exposure to advertising and self-reported alcohol consumption and alcohol-related problems, analyses of the impact of restrictions on alcohol advertising, and experimental studies of the effects of alcohol advertising. Many of these studies were considered to have inadequate data or methodological shortcomings; they could have failed to uncover a relatively small but important effect because the data were insufficient to separate the effect of advertising from other changes that were occurring. The authors of the literature review are careful to note that the literature does not justify a conclusion that changes in advertising expenditures have no effect on total alcohol consumption.

One criticism of the econometric model is that these studies examine alcohol abuse outcomes separately from alcohol consumption levels, "a critical distinction for policies aimed at minimizing misuse and abuse of alcohol." Another is that this model discounts the behavioral mechanisms by which exposure to alcohol advertising influences individual drinking behavior (Strickland 1981).

Research on the association between exposure to advertising of alcoholic beverages and consumption of alcohol by teenagers is inconclusive. In one study, teenagers who had been most heavily exposed to alcoholic beverage advertising in magazines and on television scored higher on each measure of an alcohol consumption survey than other teenagers who had been less heavily exposed (Atkin

<sup>1</sup> Field experiences identified in the cited studies referred to all activities related to the courses that took place outside of the classroom such as police-ride-a-longs, site visits to treatment centers, planning and implementing campus alcohol awareness activities, lobbying for alcohol serving policy changes on campus, serving as a student counselor (peer) at student health center, and other activities.



et al. 1984). Subjects assessed how much advertising they had been exposed to in each medium in their replies to survey questions. Teenagers who had not yet drunk alcohol but who had been heavily exposed to alcohol advertising were more likely to believe they would drink in the future than were other nondrinking teenagers who had been less intensively exposed to the ads. Overall, results from this survey indicate that teenagers' exposure to alcohol advertising is significantly associated with intentions and behavior regarding alcohol (Atkin et al. 1984). However, this same study indicated that the *most* powerful correlate of beer drinking is peer influence, followed by exposure to advertisements for beer (Atkin et al. 1984). Peer influence is also related to wine drinking but to a lesser extent than for beer; liquor consumption is more strongly associated with age and less so with peer influence (Atkin et al. 1984).

Another study looked at the impact of advertising on teenagers within the framework of social learning theory. This analysis of the effects of televised alcohol advertising on the alcohol consumption of teenagers found that advertising had meager effects on the level of consumption, and that these effects were not translated into effects on alcohol-related problems. In contrast, peer influence was found to have a significant impact on consumption levels and alcohol abuse behavior (Strickland 1983).

A nationwide survey of 1,200 respondents ages 12 to 22 found a moderately positive correlation between the amount of day-to-day exposure to ads for beer, wine, and distilled spirits, on the one hand, and alcohol consumption and drinking in dangerous situations, on the other. These relationships remained significant when demographic attributes and interpersonal influences were controlled (Atkin et al. 1983).

In an earlier study, Atkin and Block (1981) found that alcohol advertising is associated with increased consumption among adults and serves as a significant informal source of socialization about alcohol for youth. This study also found a positive association between exposure to advertising and reported problem drinking. "To some extent, these relationships may be due to reverse causation; nevertheless, it is likely that some impact is traceable to advertising" (Atkin and Block 1981).

According to Wallack (1984b), the findings that indicate an association between advertising and increased consumption contradict a larger body of previous research that has generally failed to indicate such a relationship.

It is difficult to measure the effects of advertising of any product because advertising is just one element of a marketing mix that consists of price, quality, assortment, and distribution (Van Iwaarden 1983). In addition, the manner in which publicity is applied to this mix is influenced by product life cycle, price competition, and market structure (Simon 1967, cited in Van Iwaarden 1983).

### *Content Analysis*

It is not known to what degree implicit messages of alcohol advertising influence consumption. Some research-

ers assert that the content of alcohol advertising in national media is intended to persuade vulnerable subgroups of the population, such as young people, or target segments of the population, such as blacks, to use these products. To these ends, the researchers claim that alcohol advertising is misleading and uses appeals such as "indirect promises" of increased self-esteem, wealth, peer acceptance, and sexual prowess to promote alcohol while providing no information about the risks of alcohol beverage consumption (Breed and DeFoe 1979; Atkin and Block 1981).

Other researchers cite the methodological shortcomings of these studies and discount their findings. Strickland (1984) argues that the research procedures are weak in areas such as coding procedures, definitions or content categories, sampling procedures, and measures of exposure to advertising (Strickland 1984). Strickland et al. (1982) conducted a study that was set up to replicate Atkin and Block (1981) while at the same time partially correcting some of the methodological weaknesses of their study. The Strickland et al. (1982) study analyzed the themes, appeals, techniques of presentation, and use of human models in 3,131 beverage alcohol ads in 454 national magazines. The findings indicate that the major themes frequently used were quality of the product and heritage or tradition. There were a disproportionately high number of alcohol ads in black-oriented magazines, thereby exposing these readers to a heavy concentration of alcohol advertising. However, in youth- and women-oriented magazines there was very little alcohol advertising (Strickland et al. 1982).

Wallack (1983), in an attempt to bring reason to the controversy and neutralize the conflict, concludes:

Analysis of content and effects cannot be separated from the larger marketing mix of price, physical availability, and general institutional and social support for drinking. ...Such analysis cannot be separated from researchers' disciplinary training and the values inherent in their backgrounds....(p. 14)

The arguments on both sides of this issue may have merit, but there is little definitive empirical evidence to settle the question.

### *Other Media Portrayals*

A prevention measure believed to have merit is reducing the use and glamorization of alcohol in the mass media, or at least increasing the realistic portrayal of the deleterious consequences of alcohol consumption. There is a widely held assumption that drinking scenes in media can bring about increased consumption by viewers or mistaken beliefs about the prevalence and situations of use and consequences of alcohol consumption. This is based on concern that the media help to create social expectations and norms that drinking is appropriate in virtually all situations and that drinking is expected.

Although the empirical studies on this issue are inconclusive, there remains widespread support for and success in limiting the drinking scenes in the entertainment media and for using the entertainment media for alcohol prevention education (Breed and DeFoe 1982; Wallack et al. 1985).



According to social learning theory, viewers who are frequently exposed to consistent content stimuli can be affected by that exposure (Wallack 1984a). A statement by Greenberg et al. (1979, quoted in Wallack 1984a) is illustrative:

To the extent that social behaviors on television, such as acts of drinking, are performed...in a positive context, without negative consequences, or with positive rewards, social learning is more likely to occur. Such learning...can affect the viewers' aspirations and expectations about the observed behaviors; it can impinge on the viewers' beliefs with regard to the acceptability or appropriateness of the behavior, it can teach the behavior, and it can induce their imitation or a desire for imitation.

Virtually none of the characters of television's popular situation comedies and dramas smoke cigarettes or use illegal drugs (Greenberg 1981), but most of them do drink. In fact, they drink beer, wine, and distilled spirits more frequently than any other kind of beverage—the converse of consumption in the “real world” (Breed and DeFoe 1981). A 14-week study of the top 15 situation comedies and hour-long dramas found most drinkers were “settled adults.” Their drinking occurred most often before, during, or after a crisis. Disapproval of alcohol abuse was depicted relatively infrequently and most often by women. “Regular characters on the show netted the least frequent disapproval for their drinking and were ‘protected’ from punishment for alcohol abuse.” In terms of loss of status, harm to self and others, and other consequences of drinking, “the regular characters suffered less than the nonregulars” (Breed and DeFoe 1981, p. 67). Based on social learning theory, the relative absence of serious consequences of alcohol abuse may be especially significant (Breed and DeFoe 1981).

A 9-year study by Breed et al. (1984) revealed that the number of acts of drinking on television rose from slightly fewer than five per hour in 1976–1977 to more than eight in the 1981–1982 season. The study also studied the content of daily newspapers, college newspapers, comic books, and magazines. Alcohol played a small role in comic books except in strips featuring fantasy characters. More than half the national ads in college newspapers were for alcohol. Alcohol was generally treated offhandedly in the “lifestyle” segments of newspapers, such as feature columns and comics; and ads in newspapers were more matter-of-fact than those in magazines. Some of the newer women's magazines dealt with the potential problems associated with drinking, and business magazines emphasized an austere work ethic. High-quality literary magazines in general treated the subject realistically.

An analysis of major drinking themes depicted on a popular daytime soap opera (Wallack et al. 1985) for a 4.5-year period, along with a study of 30 consecutive program broadcasts, found several good role models for “social drinking” and abstinence. Characters who participated in heavy drinking and high-risk drinking often received negative reinforcement for those behaviors.

Two recent laboratory studies of the television programs with drinking scenes resulted in inconclusive findings. The

results of one study indicated that television programs may influence children's attitudes toward alcohol abuse (Rychtarik et al. 1983, as cited in Sobell et al. 1986), while the other study provided no support for the idea that drinking scenes in television programs precipitated drinking by viewers (Sobell et al. 1986).

## PREVENTION: LAWS AND REGULATIONS

Laws and regulations adopted by Federal, State, and local governments can influence alcohol consumption and the nature and level of alcohol-related problems. Some measures have been shown to prevent alcohol-related problems. Included in this section is a discussion of the impact of the price of alcoholic beverages, minimum drinking age laws, restrictions on availability, and drinking-and-driving laws.

### Price of Alcoholic Beverages

There is growing evidence that the price of alcohol influences both alcohol consumption and alcohol-related problems.

Cook (1981) and Cook and Tauchen (1982) found that relatively small increases in the price of distilled spirits (due to increases in State taxes) reduced not only consumption of distilled spirits but also death rates from liver cirrhosis and automobile crashes.

More recently, Grossman and colleagues have conducted a series of studies on the impact of the price of alcohol on consumption and alcohol-related problems among young people. Based on analysis of information on alcohol use by young people ages 16 to 21 obtained in the first and second U.S. Health and Nutrition Examination Surveys (HANES), Grossman et al. (in press) and Coate and Grossman (1986) conclude that higher real prices for beer, the most popular alcoholic beverage among youths, would reduce not only the number of young people who drink but also the incidence of heavy drinking and of frequent drinking.

They estimated the impact of three alternative Federal excise tax policies on beer consumption by young people with the following results (expressed as absolute changes in percentage):

- If the Federal excise tax on beer had been indexed to the rate of inflation since 1951 (causing the price of beer to rise by approximately 12 percent between 1976 and 1980, the period of the second HANES survey), the number of youths who drank four to seven times a week would have declined by 8 percent and the number who drank one to three times a week would have declined by 6 percent.
- If the alcohol in beer had been taxed as heavily as the alcohol in distilled spirits (causing an 18 percent increase in the price of beer during the sample period), the number of youths who drank four to seven times a week would have declined by 11 percent and the number who drank one to three times a week would have declined by 8 percent.



- If the Federal excise tax on beer had been indexed to inflation since 1951 and if the alcohol in beer had been taxed as heavily as the alcohol in distilled spirits (causing a 57 percent increase in the price of beer during the sample period), the number of youths who drank four to seven times a week would have declined by 32 percent, the number who drank one to three times a week would have declined by 24 percent, the number who drank less than once a week would have declined by 8 percent, and the number who did not drink beer at all would have increased by 28 percent.

Saffer and Grossman (1985) analyzed the impact of State excise taxes on beer (adjusted for inflation) on motor vehicle accident mortality rates for young people. On the basis of a time-series study of State cross-sectional data for 1975 through 1981, they found that States with relatively high excise taxes on beer have lower death rates from motor vehicle accidents for youths ages 15 to 17, 18 to 20, and 21 to 24 (other variables held constant). In addition, they estimated that if the Federal excise tax on beer had been indexed to the rate of inflation since 1951, the lives of 1,022 youths between the ages of 18 and 20 would have been saved in a typical year during the sample period. This represents a 15 percent reduction in the number of persons in that age group killed in crashes.

Saffer and Grossman further estimated that if the alcohol in beer had been taxed at the same rate as the alcohol in distilled spirits, the number of 18- through 20-year-olds killed would have been 21 percent lower. Combination of the two tax policies would have caused a 54 percent decline in the number of 18- through 20-year-olds killed.

In a study of the impact of alcohol price increases in Scotland, Kendell et al. (1983) found reductions both in consumption and alcohol-related problems. Surveys of "regular drinkers" in 1978-1979 and again in 1981-1982 (after a combination of tax and price increases caused the price of alcoholic beverages to rise faster than the retail price index and average disposable income) indicate that, between surveys, total alcohol consumption fell by 18 percent and associated adverse effects reflecting an existing or developing dependency on alcohol dropped by 16 percent. The effects of other possible influencing factors, such as social class, income, and employment and marital status, were also analyzed. Although growing joblessness did somewhat affect drinking, and although the heavy drinkers surveyed seemed especially likely to become unemployed, the primary factor responsible for reducing consumption was the price of alcohol. Consumption dropped at least as much among heavy drinkers and persons dependent on alcohol as it did among light and moderate drinkers.

Ornstein and Levy (1983), in a review of econometric studies attempting to estimate the effect of price changes on demand for alcoholic beverages, note that results vary widely according to the country of study, data used, and model and statistical technique. However, they state that, for the United States, most studies have found demand for beer to be relatively price-inelastic (around  $-0.3$ ) and demand for distilled spirits to be price-elastic (around  $-1.5$ ); they found little evidence for wine. (For a price-

elastic good, elasticity is greater than 1, and a given percentage change in price causes a more-than-proportionate change in quantity demanded. For a price-inelastic good, elasticity is less than 1, and a given percentage change in price will cause a less-than-proportionate change in the quantity demanded.)

Arguing that among the reasons for disparity in results across demand studies is the "inability to incorporate properly the effects of changes in the price of one category of alcoholic beverages on consumption of another," Levy and Sheflin (1983, 1985) attempted to estimate the effects of price changes on demand aggregated over all alcoholic beverages. They estimated a price elasticity of  $-0.5$ , implying that demand is not wholly dependent on price. However, they noted that "this is large enough to indicate that price policies can be a very effective means of reducing alcohol consumption."

### Minimum Drinking Age

Research indicates that lowering the minimum age of alcohol purchase is associated with an increased rate of automobile crashes among young people. Conversely, increasing the minimum age of purchase reduces the rate of automobile crashes among young people. Many of the studies on the impact of minimum age of purchase focus on the experiences of Michigan, Maine, Massachusetts, New York, and Illinois (Ferrence and Whitehead 1975; Zylman 1976; Wagenaar 1982a, b, c, d; Williams and Lillis 1986).

#### *Impact on Traffic Crashes*

Cook and Tauchen (1984) analyzed auto fatality rates for young people during the 8 years between 1970 and 1977 in the 48 contiguous States, along with levels of availability of alcohol to young people in those States. They concluded that a reduction in the minimum legal drinking age from 21 to 18 years old for all alcoholic beverages would increase the rate of auto fatalities for people between 18 and 20 years of age by about 7 percent and by somewhat less for 16- and 17-year-olds.

An evaluation of the effects of raising the legal drinking age on crash involvement by young people in Michigan found significant reductions in that involvement (Wagenaar 1986) (see figure 1). A 6-year followup of the situation in Michigan indicates that reductions of 16 percent in single vehicle nighttime crash involvement and 19 percent in police-reported alcohol involved injury can be attributed to the legislation changing the drinking age (Wagenaar 1982b, 1986).

Fatal nighttime crashes involving single vehicles with teenage drivers dropped 5 percent in Massachusetts in the first 2 years after the minimum drinking age was increased to 20 compared with the previous 3 years; in contrast, such crashes increased by 19 percent in New York, which had retained a minimum drinking age of 18 during the same time period. When the average of fatal crashes involving teenage drivers in the 3 years before the law took effect was compared with the average in the 2 years after its adoption, the figures in Massachusetts dropped 1 percent and in New York rose by 5 percent (Hingson et al. 1983).



Most studies of the minimum drinking age emphasize the role of males in drinking and driving crashes; little research has been conducted to shed light on the involvement of females. In a study conducted to find empirical evidence to support 19 as the minimum age of purchase for New York, Lillis et al. (in press) analyzed the role of 18-year-old females in drinking-and-driving crashes. They concluded that 18-year-old female drinking drivers were involved in crashes resulting in casualties.

The National Highway Traffic Safety Administration (Arnold 1985) compared the number of fatal crash involvements per year per affected driver after the legal minimum drinking age was raised with the number before the law was changed. During the years 1975 through 1982, 15 States increased the minimum drinking age. Data from 13 of these States were analyzed; combined figures indicate a net effect of 13 percent fewer fatal crash involvements. Figures from the individual States reveal that fatal crash involvements among drivers affected by the legislation ranged from a 29 percent reduction to a 14 percent increase. Reductions in fatal crash involvement were significant in Florida, Michigan, and Minnesota.

A study compared the automobile fatalities from 1975 to 1979 in nine States that raised the minimum age of purchase during this period with nine States that did not. The results were a 41 percent decrease for all drivers in nighttime single-vehicle fatalities and a 30 percent decrease among the group affected by the age change (Williams et al. 1983).

Researchers have studied the automobile fatalities of 26 States that raised the minimum purchase age between 1975 and 1984. The findings showed a 13 percent reduction in nighttime fatal crashes among 18- and 19-year-old drivers, the affected age group. The effect was consistent across regions and stable over time. The reduction effect was greater for females than for males, 26 and 10 percent, respectively (DuMouchel et al. 1985).

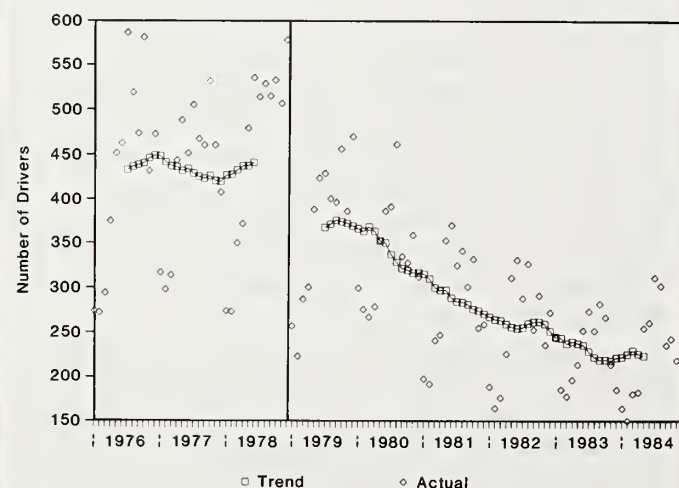


FIGURE 1. Police-reported drinking drivers ages 18 to 20 involved in crashes including at least one injury or fatality, State of Michigan.

SOURCE: Wagenaar 1986.

Saffer and Grossman (1985), in an analysis of State data from 1975 to 1981 paralleling their analysis of the effects of higher excise taxes on beer, explored the effect of the minimum legal age for the purchase of beer on motor vehicle fatalities among young people ages 15 to 17, 18 to 20, and 21 to 24. They found that the motor vehicle crash death rate of 18- to 20-year-olds is inversely related to the minimum legal age for purchase of beer. In addition, they estimated that a drinking age of 21 for beer in all States would have reduced the number of 18- to 20-year-olds killed in motor vehicle crashes by 8 percent in the period from 1975 through 1981; this percentage translates to 555 lives that might have been saved. This finding suggests that higher beer prices realized through taxation combined with drinking-age policy are powerful forces in reducing automobile fatalities.

In a review of studies on raising the minimum drinking age, Vingilis and DeGenova (1984) concluded that the laws may have some effect in reducing consumption, alcohol-related problems, and collisions. Although young people drink, their mean level of consumption and alcohol-related problems can be shifted upward and downward with legal controls.

Little is known about the potential effects of raising the drinking age on people immediately younger than those targeted by the law. Specifically, does increased distance from the age at which alcohol can be legally purchased produce an observable effect on drinking-and-driving behavior and crash involvement of 16- and 17-year-olds?

### *Impact on Alcohol Consumption*

Empirical evidence on the impact of minimum purchase age on consumption and drinking patterns of young people is growing. An analysis of the sales of beer, wine, and liquor in Maine after the drinking age was lowered from 20 to 18 in 1971 found no important changes in the figures for any of the three drinks. After the age was raised to 20 again late in 1977, however, beer sales declined substantially. In New Hampshire, beer sales increased significantly when the legal drinking age was lowered from 21 to 18 (Wagenaar 1982c).

A four-part study conducted in the Province of Ontario, Canada, to discern the impact of a 1-year increase in the minimum purchase age found that the law had a minimal effect for 18- to 19-year-old high school students but none for the regular drinkers (once a week or more) or for younger drinkers. The 1-year increase in minimum age was not sufficient to cause a major impact on youthful drinking behavior (Vingilis and Smart 1981).

Hingson et al. (1983) compared the alcohol consumption of a large sample of young people between 16 and 19 years of age in Massachusetts and New York State in the 2 years after Massachusetts raised its legal drinking age to 20; New York State retained the age of 18 as its cutoff point. The respondents' average, self-reported, daily alcohol consumption in Massachusetts did not decline, compared with the average for New York State residents. The proportion of teenagers who reported they drove after drinking heavily did not increase in either State, although the teenagers



in Massachusetts did report driving after drinking significantly less frequently than those in New York.

Smith et al. (1984) studied data on part of this same population—youths between 16 and 17 years of age, the group immediately younger than the group at which the law was aimed. Analysis of outcome figures indicated minimal effects on the drinking behavior of Massachusetts 16- and 17-year-olds.

Coate and Grossman (1986) examined the effects of minimum legal drinking ages on alcohol consumption by young people ages 16 to 21, on the basis of information contained in the second HANES (which was conducted between 1976 and 1980). They found that frequency of consumption of beer, the most popular alcoholic beverage among youths, is inversely related to the minimum legal age for its purchase and consumption. They estimated that a uniform minimum drinking age of 21 for beer in all States would have reduced the number of youths who drank beer four to seven times a week during the sample period by 28 percent and the number who drank one to three times a week by 11 percent; the number who did not drink beer at all would have increased by 14 percent (and the number who drank less than once a week by 2 percent).

In a review of the literature on minimum drinking age, Holder (1985) reports that

The basic assumption of any change in drinking age is that the amount and/or the pattern of drinking by the young will be altered. Few studies have analyzed the changes in consumption patterns which can be attributed to minimum age change. This results from a lack of available longitudinal data concerning adolescent drinking; most studies rely on self-reported consumption. Such surveys have not always produced consistent conclusions concerning the effect of minimum age change on youthful consumption (p. 16).

### Other Restrictions on Availability

Research into the physical availability of alcoholic beverages, as measured by hours and days of sales, density of outlets, and other restrictions on distribution, has resulted in varying findings.

#### *Availability, Consumption, and Alcohol-Related Problems*

Much of the empirical literature on alcohol-related problems has focused on physical availability as a predictor of levels of alcohol consumption. Availability is studied as a function of location, type, and density of outlets. Macdonald and Whitehead (1983) found that consumption rates are positively related to the number of off-premise outlets. The evidence of a relationship between on-premise outlets and per capita consumption is limited (Maynard 1983; Ross and McCleary 1983). The cost of alcoholic beverages sold on-premise is substantially higher than the cost of off-premise beverages, and this may make on-premise consumption less sensitive to changes in availability than off-premise consumption is (Macdonald and Whitehead 1983).

Although much of the literature on availability discusses

physical availability, this research is not sufficient to understand availability as it applies to the individual consumer (Rabow and Watts 1982). Availability is determined both by physical and by social and psychological factors. Consumption is a function of the individual's sociocultural milieu (Smart 1980, cited in Rabow and Watts 1982). Rabow and Watts (1982), following up on an earlier study by Smart, studied the salience of social availability as it relates to consumption. The investigators found that alcohol consumption is a socially integrated practice and that various segments of the population tend to overconsume in different social situations. Specific kinds of consumption are related to social and demographic characteristics of a population rather than to mere physical availability of alcoholic beverages.

Researchers examining alcohol availability and alcohol-related problems employed the sociocultural model in a study of 213 California communities. They found that both on-premise and off-premise outlet availability, inclusive of sociodemographic variations, does have a significant impact on each of the alcohol problems considered—felony drunk driving, misdemeanor drunk-driving arrests, and cirrhosis mortality rates (Watts and Rabow 1983).

In an earlier study of 50 California counties, Watts and Rabow (1983) found that greater cirrhosis mortality rates between 1971 and 1974 were associated with only one type of on-premise availability—density of beer outlets. This study did not control for sociodemographic factors. Together, the two studies suggest that the relationship between cirrhosis mortality and density of outlets can best be explained through using factors such as age and race.

Colon and Cutter (1983) studied the relationship between motor vehicle fatalities for 1 year with density of on-premise outlets and beer consumption. They found that motor vehicle fatalities were positively related to beer consumption but negatively related to density of on-premise outlets.

Colon (1981) examined consumption and its relationship to alcoholism. Using a quasi-experimental multivariate analysis controlling for sociodemographic factors, the study found that the rate of alcoholism was influenced by urban conditions and a social isolation factor, "isolated females." Consumption was not a significant predictor of alcoholism.

Rush et al. (1986) applied a statistical technique called analysis of linear structural relations (LISREL) to a set of data from Ontario, Canada, concerning the availability of alcohol, its consumption, and damage related to alcohol consumption. Results of the investigation supported the existence of specific causal paths that are consistent with the distribution of a consumption model (which postulates that the availability of alcohol has a direct causal effect on the aggregate level of alcohol consumption in a given population and, thus, an indirect effect on alcohol-related problems). The authors concluded that restricting the availability of alcohol will reduce per capita rates of consumption as well as reducing mortality and morbidity related to alcohol in the general population (Rush et al. 1986).



### *Impact of Specific Changes in Availability*

A number of studies have reported some important effects on alcohol consumption and alcohol-related problems when the availability of alcohol has been modified.

Public consumption of alcohol has been available in most states since the end of Prohibition. However, the role of public drinking and alcohol-related problems has been difficult to isolate. Holder and Bloise (in press) found that permitting the sale of liquor-by-the-drink in North Carolina resulted in a 6 to 7 percent statistically significant increase in overall distilled spirits sales. Using time series analysis, Bloise and Holder (1987) found that alcohol-related traffic crashes increased from 16 to 24 percent when liquor-by-the-drink became available. In an overall assessment of this change in distilled spirits availability, Bloise and Holder (in press) concluded that while there was evidence of some shift in self-reported on-premise beer and wine consumption, the changes in spirits consumption was more the result of some combination of additional new consumption and a shift from off-premise consumption for some or all beverage types to the on-premise consumption of liquor.

When Idaho, Maine, Virginia, and Washington made wine available for sale in grocery stores, wine consumption rose significantly more than would have been expected based on prior trends in each of the four States except Virginia (Macdonald 1985). Consumption of beer and liquor was also analyzed, and consumers were not found to be substituting wine for either of the other two beverages.

A longitudinal analysis of restrictions on the availability of alcohol in the United States between 1955 and 1980 found that certain regulatory mechanisms have played a significant role in reducing consumption of distilled spirits (Hoadley et al. 1984). Specifically, restricting the sale of liquor by the drink and maintaining dry areas within States deterred consumption. Restricting the times when alcohol could be sold produced unexpected results: preventing sales of alcohol on Sundays had no noticeable effect, whereas earlier closing of establishments offering alcohol for sale was associated with more sales, not less. Raising the prices for alcohol was found to have the greatest effect in lowering consumption.

In Norway, a strike at the Norwegian Wine and Spirits Monopoly halted deliveries of wine and liquor to retailers and licensed premises for 9 weeks in 1978. Sales of beer, imports of wine and liquor, and the production of wine and spirits by consumers at home all increased. Nonetheless, the supply of alcohol decreased about 10 to 15 percent, and total alcohol consumption dropped by an estimated 5 to 10 percent. Indicators of alcohol-related problems, such as admissions to detoxification facilities, arrests for drunkenness and related offenses, and domestic violence, dropped dramatically (Horverak 1983).

A strike by miners and steelworkers in the Sudbury basin in Ontario, Canada, 1978-1979, produced an overall decline in alcohol consumption for the 8.5-month strike (Giesbrecht et al. 1982). In the city of Sudbury, the proportion of alcohol sold as beer rose slightly in relation to wine and

liquor. The outcome supported the hypothesis that lower disposable incomes would reduce alcohol consumption. At the same time, however, the proportion of beer sales made by licensed establishments (i.e., taverns and pubs) in the city of Sudbury remained stable.

### *Drinking-and-Driving Laws*

Increasing the probability of detection and punishment for drinking and driving reduces traffic crashes and resulting injuries and fatalities. The public's perception of that probability is considered important to the long-term effectiveness of drinking-and-driving laws.

#### *Methods for Studying the Impact of Drinking-and-Driving Laws*

Ross and McCleary (1983) examined the correlational, quasi-experimental, and experimental study designs used by researchers to examine causal connections between drunk driving and legal interventions. They consider the time series to be the strongest of the quasi-experimental designs. This design employs data that are acquired cheaply from official sources, and because it can overcome the common threat to inferential validity that is a weakness of other designs, it is recommended as a model for the study of deterrence of drinking and driving.

Heeren et al. (1985) looked at surrogate measures of alcohol involvement in fatal crashes to determine which measures used were most likely to reflect alcohol involvement in fatal crashes. They concluded that nighttime fatal crashes are the best surrogate measure of alcohol-related crashes. However, the authors acknowledge that surrogate measures may not accurately measure trends in alcohol-involved crashes over time, particularly in small States or over short durations. The most accurate way to assess the effects of drunk-driving countermeasures is to test all drivers involved in fatal crashes for blood alcohol level.

#### *Impact of Law Enforcement on Traffic Crashes*

Drinking-and-driving laws are believed to be effective deterrents if they provide for certain, severe, and swift punishment (Ross 1984).

Sobriety checkpoints may increase the perceived certainty of punishment for alcohol-impaired driving. Significant decreases in alcohol-related crashes and traffic deaths have been reported for periods when checkpoints have been in effect (Ross 1985). Comparisons of public perceptions in areas where checkpoints were and were not in use show that the likelihood of arrest for alcohol-impaired driving is considered greater in checkpoint areas; despite differences in estimates of the risk of punishment, however, there were no differences in reported drinking-and-driving behavior between residents of checkpoint and comparison areas (Ross 1985). Although the chances of arrest were perceived to be higher in the checkpoint areas, they may have still been too low to persuade drivers to abstain; considerably more checkpoint activity may have been required to attain a deterrent effect (Ross 1985).



Experience suggests that enforcement can be most effectively implemented in jurisdictions with per se laws, which mandate the use of roadside screening devices and some form of breath testing (Jonah and Wilson 1983).

Drinking-and-driving laws in Norway and Sweden have served as a model for similar laws in Europe, Australia, New Zealand, and North America. Both Sweden and Norway employed blood alcohol testing and set fixed blood alcohol limits to provide conclusive evidence, per se, of drunken driving (Snortum 1984). Scientific evidence gathered over a period of 50 years indicates a direct relationship between increasing blood alcohol concentration (BAC) in drivers and increasing risk of a motor vehicle crash. According to a scientific consensus, alcohol causes deterioration of driving skills beginning at 0.05 percent (Council on Scientific Affairs 1986). The American Medical Association supports a policy recommending adoption by all States of 0.05 percent BAC as per se evidence of alcohol-impaired driving.

Hingson et al. (in press) studied the effects on crashes of Maine's 1981 drunk-driving law, considered one of the toughest in the Nation. The law introduced a civil charge for driving while impaired (DWI) so that the State needed to prove only preponderance of evidence rather than guilt beyond a reasonable doubt; a blood alcohol level of 0.10 became per se evidence of driving under the influence of alcohol. Previously convicted alcohol-impaired drivers were no longer allowed second jury trials, and minimum mandatory penalties were established.

During the first year after the law was passed, there were increases in DWI arrests, an 85 percent increase in the conviction rate, and increased perceptions by the police and the driving public that alcohol-impaired drivers would be stopped, arrested, convicted, and given automatic fines, license suspension, and jail sentences. During the first 2 years after the law was in force, significantly more Maine drivers decided not to drive after drinking, in comparison with respondents from other New England States. Fatal crashes and single-vehicle nighttime crashes declined 35 percent; this decline was significantly greater than in other New England States during the same period.

Three years after enactment of the law, however, drivers less frequently made decisions not to drive after drinking and fatal crashes returned to the pre-1981 level. Also by the third year, the public no longer regarded the penalties as severe. Even though alcohol-impaired drivers who were arrested were more likely to be convicted in Maine, so few were stopped and arrested that the perceived likelihood of being punished for alcohol-impaired driving was not great. Thus, even with an increase in conviction rates, the law was unable to achieve a sustained reduction in alcohol-impaired driving and fatal crashes. It is unclear what effect the discretionary authority of the police to stop and arrest alcohol-impaired drivers had on the overall impact of the law (Hingson et al. in press).

Holder and Blose (1983) employed a computer simulation model using research data from various studies to evaluate potential intervention strategies to reduce alcohol-related traffic problems in three counties in North

Carolina, Vermont, and California representing rural, urban, and mixed populations. The drinking-and-driving strategies that were simulated were as follows: (1) lowering the legal blood alcohol content to 0.08 percent, (2) increasing drivers' perceived risk of arrest and conviction for DWI fivefold, (3) increasing the actual level of enforcement by 25 percent, and (4) increasing the DWI conviction rate by 50 percent.

The computer simulation found that increasing the perceived risk of sanctions against drinking and driving had a significant but short-term impact, whereas increasing actual sanctions without purposefully raising perceived risk had little impact. Drivers' perceived risk of arrest and conviction was the primary influence on driver behavior. None of the simulated drinking-and-driving strategies had a significant long-term impact on traffic fatalities in the model. Although an increase in perceived risk of arrest and conviction was followed by an immediate small drop in fatalities, the toll rapidly returned to the baseline level. The investigators suggest that repeated attempts to alter perceived risk, perhaps at 5-year intervals, may be worth further consideration (Holder and Blose 1983).

### *Severity of Punishment*

License revocation may have a deterrent effect because there is evidence that it is perceived by the public as a relatively severe sanction (Waller 1985). However, increasing the severity of other types of penalties for DWI offenses appears to have little long-term deterrent effect. Mandatory jail sentences for DWI are on the books in at least 25 States, in many instances even for first-time offenders. The evaluations of these programs that are beginning to be reported indicate that delays and postponements of trials, failure of defendants to appear, a decreasing number of convictions in response to pleas of innocence, and case dismissals tend to distort the criminal justice system; although offenders found guilty are almost always sent to jail, a large proportion of the accused are freed (Haddon and Blumenthal 1984; Ross 1985). Any program that greatly increases the rate of DWI arrests must be supported by a judicial system that can handle the additional burden of cases. The problem could be partly alleviated by revising the penalty structure in such a way that an optimal balance between severity and certainty of punishment is achieved (Jonah and Wilson 1983).

### *Swiftness of Punishment*

License revocation, when tied to an administrative rather than criminal hearing, is designed to make punishment swift and certain, the key variables in the deterrence approach. Administrative license revocation was enacted first in Minnesota and subsequently in several other States. Under typical legislation, the driver's license is collected from an offender by an officer at the time of arrest if the offender refuses to submit to a test of blood alcohol content or if the test shows a BAC of 0.10 percent or more (Waller 1985). The motorist is issued a temporary permit valid for a few days and may request judicial review but only after the revocation has gone into effect. There are



indications that Minnesota drivers believed that risk of apprehension and punishment was increased by this legislation, but at present there are no studies demonstrating that administrative license revocation actually is a deterrent to drunk driving (Ross 1985; Waller 1985).

### *Impact of Publicity About Laws on Traffic Crashes*

Publicized campaigns of enforcement for drunk-driving laws are also based on a belief in the perceived certainty of threat. The "Cheshire Blitz" (increased print and electronic media coverage) was used in 1975 to apply the British Road Safety Act of 1967. As a result, there was a statistically significant decline in serious crashes (Ross 1984, citing Ross 1977).

Mercer (1985) conducted a correlational examination of data from British Columbia on the relationships among the number of vehicles checked in police drinking-and-driving road checks, the number of driving-while-impaired charges laid, the number or percentage of alcohol-related casualty traffic crashes, and the extent of media coverage on drinking and driving as measured by the print media. The study revealed that the extent of media coverage, not the extent of road checks or charging activity, is probably the critical element in the reduction of drinking-and-driving crashes.

### *Education and Rehabilitation of Drinking Drivers*

Research has found that educational or rehabilitative programs may have marginal positive impact on DWI recidivism, compared with no intervention or sanctions at all (Hagen 1985), but that license revocation is a more effective countermeasure for reducing driving by impaired drivers (Waller 1985). Drivers convicted of alcohol-related offenses have fewer crashes after having their licenses suspended or revoked than after being sent through rehabilitation programs (Haddon and Blumenthal 1984).

Licensing sanctions appear to have a greater positive impact on traffic safety than educational or rehabilitative measures (Hagen 1985), such as schools for alcohol-impaired drivers, group therapy, and treatment for general alcohol abuse. These latter approaches do not reduce future crashes of persons arrested for DWI any more than traditional punitive treatment (Reed 1982). Further research is needed to define the most appropriate uses of educational, rehabilitational, and legal coercive approaches in dealing with this group.

In an evaluation of the California Drunk Driving Countermeasure System, Sadler and Perrine (1984) analyzed driving records of repeat DWI offenders for 4 years after arrest. In the demonstration counties, 2,534 repeat offenders entered a 12-month pilot alcohol abuse rehabilitation program in lieu of license actions. The remaining 2,420 offenders in the demonstration counties received either 12-month suspensions or 3-year revocations of their driver's licenses. In comparison counties, 2,866 repeat DWI offenders received license actions.

Those who received license actions had significantly fewer nonalcohol-related crashes and convictions than did participants in the rehabilitation program; nonalcohol-related crash and conviction rates were about 70 percent higher for the rehabilitation group, a difference attributed to more cautious driving by people subjected to license actions and reduced driving exposure. Only 50 percent of those whose licenses were suspended were able to fulfill the proof of insurance requirement and therefore able to get their licenses reinstated.

Although participants in the rehabilitation program had 9 percent fewer alcohol-related convictions than the license-action group, no significant differences in alcohol-related crashes were found between the rehabilitation program participants and license-action recipients. However, the investigators point out that prestudy differences in crashes and convictions suggest that recipients of license actions had greater risk of recidivism when the study began, so the results may be somewhat biased. Neither approach seems to have had a substantial impact on subsequent DWI involvement, as more than 40 percent of all DWI offenders in the study had at least one subsequent conviction for an alcohol-related traffic offense during the 4-year followup period.

In terms of total crashes, both alcohol-related and nonalcohol-related, the rehabilitation program participants had a significantly higher (30 percent) 4-year rate than the license-action group. The investigators conclude that even though neither approach appeared to have much impact on DWI recidivism, license-action countermeasures provide some advantage by reducing nonalcohol-related crashes and convictions, whereas rehabilitation in lieu of license action does not. They suggest that some alternative other than license-action waivers should be used to induce repeat DWI offenders to participate in treatment (Sadler and Perrine 1984).

Mann et al. (1983) conducted a critical review of the effectiveness of rehabilitation programs. They conclude from the research reviewed that rehabilitation programs may have a beneficial impact on traffic safety measures, but they were not able to identify with any certainty the effective programs. Also, most programs reviewed showed no effectiveness in modifying treatment lifestyle measures. They conclude that the effectiveness of rehabilitation programs has yet to be established. Although many of these programs exist, few other than the Alcohol Safety Action Projects have been evaluated.

### *Limitations of Methods for Studying the Impact of Drinking-and-Driving Laws*

Ross and McCleary (1983) examined the methods used by researchers to study the impact of drunk-driving laws based on the deterrence model. They conclude that the time-series quasi-experimental design is the most effective in detecting changes that may occur from simple deterrent measures. This design is not suited for assessing gradual or cumulative effects (Snortum 1984).



Different research methodologies seem to generate slightly different conclusions about the ability to control alcohol-impaired driving. The concept of deterrence is inadequate because it is not clear by which processes it is expected to operate (Goodstadt 1983). There is empirical evidence that suggests that extralegal factors such as moral beliefs and informal social sanctions have more influence on behavior than do legal factors (Goodstadt 1983; Pater-noster et al. 1983; Pestello 1984; Williams 1985).

In deterrence research, lack of misbehavior has been treated as if it indicates a fear of consequences. An examination of this idea suggests that "compliance to rules may be a phenomenon separate from fear. Individuals may perceive the elements of the sanctioning system as threatening, but still be disposed to violate the rules for a variety of reasons." Perceptions of punishment are only important in the control of misbehavior because of the impact on one's perception of the fear of consequences. It is the fear that has direct effect on misbehavior (Pestello 1984).

Simple deterrence is hard to establish and harder to maintain. There are many reasons for failure to maintain long-term effects. Various problems underlie low objective risk of apprehension: "inadequate enforcement, temporary enforcement, over-reliance upon publicity in lieu of enforcement, and the high social and political costs of adequate enforcement" (Ross 1982, cited in Snortum 1984).

Changes in the risk of detection do not seem to be perceived by individuals, and differences in the perception yield no differing behavioral response. This, however, does not "preclude the importance of law enforcement in the long run, preservation of the operating constraints, moral codes and a widespread habit of separating drinking from driving" (Norstrom 1983).

Although there are empirically recognized limitations, drinking-and-driving laws based on the deterrence model appear to be a useful and promising measure to reduce the number of alcohol-involved fatal crashes. A body of empirical evidence developed from a number of different kinds of quasi-experimental studies supports this conclusion.

### *Other Measures to Reduce Alcohol-Related Traffic Fatalities*

There is a growing realization of the importance of nonalcohol-related measures to reduce all highway vehicle fatalities, not just those caused by drinking and driving. Some researchers argue that the move should be toward vehicle crashworthiness and the use of passive restraints such as self-fastening seat belts or air bags, or other safety devices such as penetration-resistant windshields, padded dashboards, energy-absorbing and other injury-absorbing packaging and steering assemblies (Cameron 1979; Vingilis 1985). It has been known since the early 1940s that the body could be "crash packaged" so that most injuries fatal to vehicle occupants would not occur (Haddon 1983). The creation of nonlethal roadside environments can reduce the severity of injuries (Holcomb 1983, cited in Cameron 1979).

## INTERVENTION

Intervention includes measures aimed at the identification of persons or groups whose drinking behavior places them at risk and of persons in the early stages of destructive drinking practices. The purpose of intervention measures is to attempt to reverse the early stages of dysfunctional drinking by individuals or by homogeneous groups at risk. (Cohen 1982, p. 127)

Many of the measures discussed in this section are promising but have limited empirical support. The measures discussed are directed at both the chronic, problem drinker as well as the high volume per occasion drinker who is at risk of injury or accidental death but may not be alcoholic.

### *Training of Primary Health Care Providers*

The medical profession has been criticized for ignoring drinking problems among patients. It is usually the primary care provider who provides the initial intervention for all the patient's health problems, but this has not been the case with alcohol-related problems. In one study (Hingson et al. 1982), 70 of 271 problem drinkers were found to have been seeing a physician for various reasons at the time the patients first noticed their drinking problem. Only 45 percent of those seen by a physician, however, were asked about their drinking, and only one-fourth of these were either encouraged to reduce their intake or warned about the health hazards of drinking. Only 3 percent of this group of heavy drinkers were referred by physicians to an alcohol treatment program.

Members of the medical community have a special opportunity to provide education to their patients about alcohol abuse. Kamerow et al. (1986) point out that primary care physicians have had little success in treating or diagnosing alcohol abuse, other drug use, or mental disorders. Inadequate training in medical school in these areas, resistance on the part of patients, and economic constraints of the health care system are suggested as barriers to greater efficacy in this area.

Some physicians appear to have a negative attitude toward alcoholics. Kinney (1983) identifies two major forces that militate against alcoholism education within the medical school curriculum. First, the structure of academic medicine, based on the infectious disease approach, is not designed for chronic behavioral problems. This approach is good for teaching about the disease state as long as it is narrowly defined by specific organ or system pathology. Medicine has been less successful in integrating the behavioral components of diagnosis, management, and therapeutic intervention. Second, alcoholism treatment emerged and grew outside the medical profession. The problem is compounded by the fact that the alcoholism field is "craft oriented" and the clinicians are expert not in academic terms but in extensive clinical experience (Kinney et al. 1984).

The problems of alcohol abuse and alcoholism are, however, receiving increased emphasis in medical school curricula. The Career Teacher Program, jointly sponsored



by the National Institute on Alcohol Abuse and Alcoholism (NIAAA) and the National Institute on Drug Abuse (NIDA), has been the impetus for many of the new courses or expanded substance abuse curricula at 60 medical education institutions (Holden 1986).

Changing physicians' attitudes about the alcoholic through increased knowledge may not necessarily lead to a change in clinical practice. Expressed attitudes often differ from behavior. Assessment of clinical behavior has been neglected in evaluating alcohol training for professionals (Weiner et al. 1982).

Barnes et al. (1984) designed and taught a course on the early detection and outpatient management of alcoholism for medical residents of five Boston area teaching hospitals. This course differed from other courses on alcoholism that emphasized changing physician attitudes because it was designed to change the clinical practice behavior of residents. As a result, 74 percent of the residents thought their skill in diagnosing alcoholic patients had improved, and 64 percent rated their management of alcoholic patients as improved.

Inclusion of a systematic drinking history in patient charts provides a sensitive yet simple behavioral marker. At Boston City Hospital, a Ten Question Drinking History (TQDH) was incorporated into an obstetrical intake procedure and used to monitor staff behavior. This pilot study demonstrated that awareness of alcohol consumption in the population of pregnant women increased when alcohol training was included in the obstetrical department's orientation program. The TQDH provided a standardized objective measurement of behavior that could be used to measure changes over time (Weiner et al. 1982).

The challenge now is to take what has been learned in substance abuse medical education and focus on strategies for further curriculum development. Recommendations have been developed (*Consensus Statements* 1985) to strengthen medical education in substance abuse for physicians in family medicine, internal medicine, pediatrics, and psychiatry. Some progress has been made by the inclusion of substance abuse education into the medical school curricula. For significant changes to occur in education and practice, national professional associations must define their roles and responsibilities.

Appropriate clinical behavior toward the alcoholic patient is the ultimate objective of professional education programs. Adequate knowledge, skills, and attitudes are needed for proper therapy. Physicians should not be singled out for attention. Nurses, nurse practitioners, physician assistants, and other primary health care providers also have a responsibility to increase their knowledge and skills on substance abuse for the purpose of improving therapeutic care of alcoholic patients.

### In-Hospital Consultation and Liaison Programs

Hospitals can treat in a sophisticated way the physical problems that develop from excessive drinking or alcoholism, but hospital staff tend to avoid dealing with the drinking behavior (Lewis and Gordon 1983). Among the myriad reasons for this avoidance may be the negative

attitude of health care professionals about abusive drinking and alcoholism, which will limit their ability to diagnose and treat alcoholic patients.

Hospital staffs' perceptions of the characteristics of alcoholics were investigated by means of a questionnaire containing a set of 23 semantic differential scales on which they rated four types of patients: the alcoholic, the non-drinker, the drug addict, and the heavy drinker. Factor analysis of the responses showed that types of patients were perceived in terms of three dimensions: stability, danger to others, and self-assertiveness. In comparison with heavy drinkers, alcoholics were perceived by hospital staff in general as unstable, harmless, and self-effacing, though clerks tended to see them as more dangerous than did professionals. Different occupational groups in hospitals have characteristic ways of perceiving addicted and alcoholic patients. A clerk is usually the first person a patient meets in a hospital. If clerks believe that alcoholics are dangerous, that attitude will be conveyed to the patient. The success a patient experiences in treatment may be adversely affected by a poor reception on the initial visit (Romney and Bynner 1985). Research studies suggest that attitudes can be improved through training (Chappel et al. 1977; Fisher 1983).

A large New England general hospital established an intervention program using an interdisciplinary team—a physician, a nurse, a social worker, an alcohol counselor, and an intake secretary. This team provides 24-hour coverage to emergency, ambulatory, and inpatient services. As a result of this training of hospital staff, the number of referrals daily from all hospital services increased. The intervention team worked with about 10 percent of all hospital admissions. As a result of the experiences of this in-hospital intervention program, guidelines for program development and a 10-point program for replication at other general hospitals evolved (Lewis and Gordon 1983).

Hospital-sponsored intervention programs serve to integrate identification and intervention of alcohol-related problems into the mainstream of a hospital's operation. The programs aid in increasing the rate of patients with alcohol-related problems who are identified, provided intervention services, and referred to community detoxification and rehabilitation services.

### Screening for Early Identification of Alcohol Abuse

Many research efforts are being directed toward developing a simple, accurate screening procedure for early identification of alcohol problems. The two major areas of investigation are biochemical markers that can be detected by laboratory tests and psychosocial indicators that can be assessed by means such as interviews and questionnaires.

Among laboratory indicators, serum levels of the enzyme gamma-glutamyl transpeptidase (GGTP) have proved to be a useful indicator of recent heavy alcohol consumption. However, the accuracy of this indicator may be affected by coexisting liver pathology, drug use, and individual metabolic differences among alcohol abusers. The



ability of serum GGTP levels to detect recent heavy alcohol use appears to be improved when interpreted in conjunction with mean corpuscular volume (MCV) and serum levels of another enzyme, glutamic oxaloacetic transaminase (SGOT) (Babor and Kadden 1985).

Other possible biochemical markers have been found insufficiently discriminating to use in population screening. It thus appears that because of the differing nutritional habits of alcohol abusers, the diversity of the biochemical systems that are affected by alcohol, and the probable genetic differences in susceptibility of those systems, no single, reliable biochemical marker of alcohol abuse drawn from current standard clinical tests is likely to be found (Babor and Kadden 1985).

A screening procedure based on 25 blood chemistry values, commonly ordered for annual physicals and hospital admissions, has been reported to distinguish among heavy drinkers, light drinkers, and abstainers (Rawlings et al. 1982; Ryback et al. 1982).

Because of differing patterns of alcohol use, most existing laboratory tests appear to have good diagnostic sensitivity only in chronic alcoholics; thus, they have limited usefulness in early intervention. However, Skinner et al. (1984) have investigated the predictive value of combining laboratory tests with clinical information obtained from a brief trauma scale consisting of questions concerning the occurrence of physical injuries. They found that a history of traumatic injury was highly sensitive to and specific in detecting excessive drinking, defined as greater than 60 grams of ethanol per day (approximately four standard drinks), in various populations, including alcoholic inpatients, alcohol or drug abuse outpatients, social drinkers, and general practice patients visiting family physicians. A history of trauma enabled the detection of 70 percent of excessive drinkers in an ambulatory population. Laboratory tests identified approximately 30 percent of the excessive drinkers but ruled out 85 percent of those without drinking problems.

An index combining the results on the trauma scale with laboratory values correctly identified 81 percent of outpatients and 86 percent of family practice patients abusing alcohol and 94 percent of outpatients and 83 percent of family practice patients who were not excessive drinkers (Skinner et al. 1984). The investigators conclude that the trauma scale can be a cost-effective screening instrument in clinical practice.

The use of the screening interview and questionnaires show promise as effective measures for early identification and intervention.

An effective device to assist the screening process is the CAGE (a mnemonic used to help the interviewer in recalling the types of questions on the questionnaire: Cutting down, Annoyance by criticism, Guilty feelings, and Eyeopeners). The CAGE is a simple four-question instrument designed to help patients recall past as well as very recent drinking situations and experiences. This device ascertains whether the person has experienced negative effects of drinking and whether other persons close to the patient have given any negative feedback about the

patient's drinking. The inquiry takes about 30 seconds to 1 minute and is included as part of the regular health screening (Clark 1981). Simple matter-of-fact questions such as the CAGE may pick up many cases of problem drinking and alcoholism that may otherwise be missed. Formal questionnaires such as the Michigan Alcoholism Screening Test (MAST) may be administered as part of routine health maintenance visits. The MAST has a high sensitivity (95 percent), so it is rarely fooled even by an alcoholic displaying heavy denial (Selzer 1971, cited in Liepman et al. 1984).

Rosett and Weiner developed a simple 10-item questionnaire (TQDH) to identify heavy drinking among obstetrical patients. These questions are asked along with other questions that become a part of the patient's medical history. The TQDH provides a systematic, objective format for assessing the level of alcohol consumption of pregnant women (Rosett and Weiner 1985).

The use of straightforward, simple questions asked when taking the regular medical history has shown promise as a strategy for identifying problem drinkers at an early stage as well as for screening for alcoholism.

### Intervention Programs for the Children of Alcoholics

As noted earlier in this report, there is good evidence that children of alcoholics are, for genetic reasons, at greater risk of developing alcoholism (see Chapter II). On this basis alone, children of alcoholics would appear to be an important focus for prevention and intervention programs. Other possible problems involving the children of alcoholics are not as clear-cut because this is a new area of study. There is a perception, however, that parental alcoholism can create an environment that leads to psychosocial problems for children and that this can lead to abusive drinking at an early age, even in the absence of a genetically transmitted susceptibility to alcoholism.

The issue of servicing children of alcoholics has grown rapidly as a major area of interest among people working in the prevention and intervention field, but programs to treat this population are new, and little research has been done to prove their effectiveness or to justify them.

Many of the questions on program format, screening for vulnerability, effects of parents' alcoholism treatment, and ethical considerations are unresolved. There are broad areas of agreement and recommendations for further research (Children of Alcoholics Foundation 1984). The report of a conference on prevention research lists areas of priority in terms of research needs, both biomedical and psychosocial (Blume 1985). There is a pressing need for an improved knowledge base from which more effective prevention programs can be developed.

There are other children who may be defined as high risk but who may or may not be identified as the children of alcoholics. They may exhibit problem behavior such as high absenteeism from school, fighting or other acts of violence, acting-out behavior, or other such deviant youth behavior. In an attempt to meet the needs of this high-risk



group, a comprehensive school-based program, modeled on employee assistance programs, has been developed in Westchester County, N.Y. (*Preventing Alcohol Problems* 1984). The program is aimed at students who are most vulnerable—pupils new to the school, seniors facing life after graduation, children of alcoholics, and others who may need special guidance in dealing with alcohol and other drug problems. Adolescents in Westchester County have easy access to highly trained counselors in the schools, where factors in drinking behavior such as drinking at an early age, poor academic performance, deviant school behavior, and poor parent-child relationships are likely to be detected. The program is considered a model for school administrators throughout the United States. It has been adopted by 29 schools in Westchester County and by many high schools in several States, as well as by the Seneca Indian Nation.

Outside evaluation of the program during its first 2 years of operation showed that during the first year there was a statistically significant improvement in school attendance among participating students whose parents were alcoholic. Compared with a control group, all participating students reported a greater decrease in alcohol or other drug use and abuse. However, only the treatment subgroup of abusing children of alcoholic parents showed significant decreases in drinking and other drug use. The second-year evaluation showed a significant decline in all levels of alcohol and drug use for participating students; a decline was also found in the control group ("Early intervention" 1983).

In contrast to the Westchester program, which used professional counselors, the Natural Helpers program developed in Washington State attempts to identify people who are already credible sources of assistance to young people and then improve their skills. The Natural Helpers program is based on the premise that students with problems tend to seek out other students and occasionally teachers or other school staff for help. The Natural Helpers program identifies these individuals and provides several days of training on evaluating a problem and referring students for help ("Early intervention" 1983).

American Indian adolescents are considered to be at high risk for alcohol-related problems. On some reservations, significant drinking problems may affect up to half the population, and alcohol abuse is considered the single most significant health problem in the American Indian community (Carpenter et al. 1985).

Peer group pressure plays an important role in promoting drinking within many American Indian communities. A peer-managed self-control program to teach responsible decisionmaking about drinking has been tested with 30 American Indian teenagers at high risk for problem drinking (Carpenter et al. 1985). Students were randomly assigned to three groups incorporating combinations of self-monitoring, peer-assisted training in self-control, and alcohol education. Significant decreases were found in quantity and frequency of drinking and in peak blood alcohol levels. These improvements were maintained at followups of 4, 9, and 12 months after intervention. Self-

reported data were verified by breath tests and official records.

## Employee Assistance Programs

Historically, work-based alcoholism interventions have increasingly become part of a broader approach, employee assistance programs (EAPs). EAPs offer identification, assessment, referral, and followup services to employees who have a wide array of problems in addition to alcohol abuse and alcoholism. These programs are implemented by management or labor or both to help troubled employees through early identification on the basis of job impairment, supervisor or union referral, or self-referral. After appropriate assessment of the problem and brief counseling, employees are referred to community resources for assistance in resolving the problem. Management goals are to reduce absenteeism, tardiness, accidents (Workers' Compensation), replacement costs, and inefficient job performance that reduces productivity.

Recent national survey data indicate that there are approximately 8,000 EAPs in U.S. organizations (Roman 1982), although the definitions and programs of these EAPs vary considerably. About 12 percent of the U.S. work force was estimated to have access to such programs as of 1980 (Walsh and Hingson 1985).

Private industry is increasingly opting for contractual provision of EAP services, in contrast to in-house programs (Straussner 1985). Straussner examined 23 New York-based companies and found that higher level employees tend to use the services provided by contractors, whereas lower level and frequently minority employees tend to use in-house programs. Contracted EAPs are perceived as better protecting the confidentiality of employees.

The central strategy of employee assistance programs is to use the performance of an employee as a basis for constructive confrontation; that is, supervisors are trained to confront an employee with evidence of impaired performance, behavior problems, or absenteeism and simultaneously offer to assist the employee in resolving the problem (Trice and Beyer 1984). The success of constructive confrontation in returning employees with alcohol problems to effective performance has been confirmed in a carefully designed study (Trice and Beyer 1984).

There is no single, generally accepted set of methods for conducting such programs, and no results are yet available from systematic research evaluating EAPs (Trice and Beyer 1984; Babor et al. 1986). Researchers find outcomes difficult to measure in tangible terms and rarely acquire access to the company records that are needed to design and carry out controlled studies (Walsh 1982). Reports from program practitioners do, however, indicate high levels of program success, and the continuing financial support of the programs by employers cannot be ignored as evaluative information (Roman and Blum 1985).

In a comprehensive review of evaluations of occupational alcoholism programs, not only did Kurtz et al. (1984) fail to find convincing evidence of the superiority of any one treatment approach, but they also questioned the



evidence that these programs do cause changes in drinking habits and job performance among their enrollees.

A major problem with the studies to date, as well as with most evaluations of EAPs, is the failure to separate the effects of EAP interventions from the treatment regimens to which employees may be referred (Roman and Blum 1985). Methodological difficulties remaining to be overcome in such studies are lack of standards for problem assessment, reliance on subjects' self-reports, variations in definition of successful outcome, lack of control groups, and very brief followup periods. A frequent and serious problem in such studies is that outcome is assessed by job performance. Although it is assumed that improvement on the job is due to reduced alcohol consumption or abstinence, consumption is rarely, if ever, determined objectively and independently. Instead, reliance is placed on the subjects' own reports of their drinking levels. Research by Orrego et al. (1979) showed that self-reports of alcohol consumption are not always reliable.

Another aspect of job-based intervention is the need to assess work environments and their potential impact on drinking behavior and drinking problems. Factors in the workplace, such as availability of alcohol, weak social controls, lack of accountability, and job stress may encourage the use and abuse of alcohol (Fillmore and Caetano 1982). Such factors may hamper an EAP's success, because a recovering employee must reenter the system that contributed to drinking problems in the first place. Research on work-based causes faces severe methodological problems; these include appropriate measurement of factors that may have causal effects, measurement of alcohol problems in nonclinic populations, and establishing cause-and-effect relationships (Parker and Brody 1982). Interventions aimed at changing the work environment are thus another means to consider in preventing job-related alcohol problems.

### Server Intervention Programs

Server intervention refers to a broad set of strategies for creating safer drinking environments by reducing the chances of intoxication and the risk that intoxicated individuals will harm themselves or others. This is a relatively new approach to reducing the development of alcohol-related problems, especially the incidence of alcohol-impaired driving. Research suggests that 50 percent of alcohol-impaired drivers are traveling from licensed establishments and are often "seriously" impaired (O'Donnell in press).

The importance of server intervention stems from its use of the environmental approach to prevention—it seeks to alter the drinking environment at the levels of the legal environment, the community environment, and the environment of a given licensed establishment. Server intervention generally incorporates server training, the development of management policies, and consideration of dram shop liability (Mosher 1983; Saltz 1985). A variety of approaches have been described (NIAAA 1986).

Server training programs, one element of server intervention, have been instituted in the hospitality industry

over the past few years and are increasingly being mandated. Few programs as yet have incorporated systematic evaluations, and little has been reported regarding the actual use of training materials or their quality. Recipients of the training increase their knowledge regarding the material presented (Mosher 1983), however, and Saltz (in press) has shown promising results in reducing the rate of consumption in an evaluation of a server intervention program on a Navy base (Saltz in press).

### SUMMARY

To some degree, alcohol abuse and its associated morbidity and mortality can be prevented. Objective measures reveal that increasing the price of alcohol and raising the minimum drinking age can be effective. Some educational programs may be successful, especially in the long run, but significantly more research is needed in this area. Changes in alcohol availability may be helpful, but more research is also needed in this area. Controversy continues over the role of advertising in alcohol consumption.

Research has shown that educational efforts for drunk drivers are less effective than license revocation. Measures to deter drunk driving may have more short-term impact, especially if the public perceives a great likelihood of being apprehended and given severe penalties for drunk driving. Server intervention, a newer approach to reducing the incidence of drunk driving, is being implemented in many communities, but the effectiveness of these programs has not yet been evaluated.

Although rigorous scientific study is lacking, occupational alcoholism programs have reported highly positive results and are being broadened into employee assistance programs offering counseling and referral services for alcohol abuse, alcoholism, and other problems that can be detected in the workplace.

Encouraging progress has been made in making physicians more aware of the importance of early detection of alcohol problems, and Federal and private initiatives have increased the emphasis on alcohol abuse education in medical school curricula.

In recent years a cultural shift has occurred regarding alcohol consumption, with many prominent citizens admitting impairment from alcohol and actively seeking help. Such a change in social attitudes should encourage other early-stage problem drinkers to get help and should make intervention efforts more effective.

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# Treatment

Data from a number of sources indicate that alcoholism treatment services and numbers of people in treatment continue to increase (Harwood et al. 1985; Noble 1985). American Hospital Association (1978, 1984) survey data indicate that total alcoholism and other drug dependency treatment units increased from 465 in 1978 to 829 in 1984 (78 percent), while total in-hospital alcoholism and other drug dependency beds increased from 16,005 to 25,981 for the same 6-year period (62 percent). The largest increase was in the private for-profit sector, where the number of units increased by 347 percent and the number of in-hospital beds increased by 392 percent from 1978 to 1984. These data are summarized in table 1.

Harwood et al. (1985) report comparative data on the ownership of services for 1978 and 1984 (see figure 1). By 1984, State and local governments owned 20 percent of 25,981 beds (a decrease of 20 percent), while investor-owned, for-profit beds increased from 5 percent in 1978 to 15 percent in 1984. Nongovernment, nonprofit control increased from 31 percent in 1978 to 44 percent in 1984. A total of 289,933 patients was estimated to be in alcoholism treatment on September 30, 1982 (NDATUS 1983), with 203,469 of these in alcoholism specialty units (see table 2). On September 28, 1984, 540,411 patients were in treatment in both alcohol only and combined alcohol and other drug dependency units. Of these, 40,786 (8 percent) were in an inpatient facility, 51,976 (10 percent) in a residential setting, and 447,649 (82 percent) were active outpatients (USDHHS 1984).

In 1984 there were approximately 34,148,000 discharges from short-stay hospitals. Of these, approximately 1,086,000 (3.2 percent) had an alcohol-related diagnosis. By 1990, the number of persons in treatment is estimated to increase by 8 percent, on the basis of projections of the 1982 National Drug and Alcohol Treatment Utilization Survey data. Most of this increase is estimated to be accounted for by almost 22,000 men and women, 21 through 44 years old.

## DIAGNOSIS, NOMENCLATURE, AND CONCEPTUALIZATION

The *Fifth Special Report to the U.S. Congress on Alcohol and Health* (USDHHS 1984) covered recent developments in nomenclature and diagnosis. In that report, attention was given to the third edition of the *Diagnostic and Statistical Manual of Mental Disorders* (American Psychiatric Association 1980) as well as to work on the International Classification of Diseases sponsored jointly by the U.S. Alcohol, Drug Abuse, and Mental Health Administration and the World Health Organization (World Health Organization 1982). This chapter does not review this work discussed in the *Fifth Special Report* but concentrates on further advances in conceptualization.

Both the *Fourth Special Report* (USDHHS 1981) and the *Fifth Special Report* (USDHHS 1984) emphasized the heterogeneity evident within and between populations of persons with drinking problems. The *Fourth Special Report* (USDHHS 1981, p. 29) noted, "These many variations in



TABLE 1. *Hospital units and beds for alcoholism and other drug dependency*

Type of hospital	1978		1984		Difference		% Change 1978 to 1984	
	Units	Beds	Units	Beds	Units	Beds	Units	Beds
Federal	97	3,884	130	5,159	33	1,275	+ 34.0	+ 33.0
State and local	133	6,356	149	5,299	16	- 1,057	+ 12.0	- 17.0
Not for profit	205	4,952	416	11,520	211	6,568	+ 103.0	+ 133.0
For profit	30	813	134	4,003	104	3,190	+ 347.0	+ 392.0
Total	465	16,005	829	25,981	364	9,976	78.0	62.0
Average bed per unit		34.4		31.0				

SOURCE: Modified from *Hospital Statistics*, 1978 and 1984 editions.

alcohol-related problems suggest that no single concept will suffice for adequate description. Categories such as alcoholism, alcohol abuse, alcohol dependence, problem drinking, and alcohol-related disabilities are of definite although limited value. Each is useful for certain purposes and certain populations, but none can represent adequately the full range of problems associated with alcohol consumption in American society."

An historical perspective readily informs us that variability among persons with alcohol-related problems, including those diagnosed as alcoholics, has been appreciated for many years. Jellinek (1960) in his classic study, *The Disease Concept of Alcoholism*, proposed a classification system consisting of five types of alcoholics. Moreover, a careful reading of the major publications of Alcoholics Anonymous (AA) (Alcoholics Anonymous World Services 1953, 1976) reveals early explicit concern with "types" of alcoholics and differences among people so labeled. Numerous early theorists and researchers have discussed the variability among alcoholics (e.g., Clinebell 1956; Jellinek 1960; Partington and Johnson 1969). While there has been inter-

est in variability among alcoholics, systematic formal research has begun only recently (e.g., Wanberg and Horn 1970).

In addition to variability among persons with alcohol-related problems, the multidimensional nature of these problems has also been recognized for some time. With regard to alcoholism, Ewing (1980), Tarter (1983), and Wallace (1985a) have all independently discussed elements of an interactive biopsychosocial model of alcoholism in which biological, behavioral, and sociocultural factors are considered essential for understanding etiology, pathogenesis, course, maintenance, and treatment.

This traditional view of alcoholism and alcohol-related problems as varied and multidimensional is explored further in this chapter in terms of recent developments. The chapter begins with a focus on continued efforts to define and assess the heterogeneity within and between populations of persons with alcohol-related problems. Also, the implications of such heterogeneity for the treatment of alcoholics are explored. Other issues concerning treatment are examined throughout the chapter.

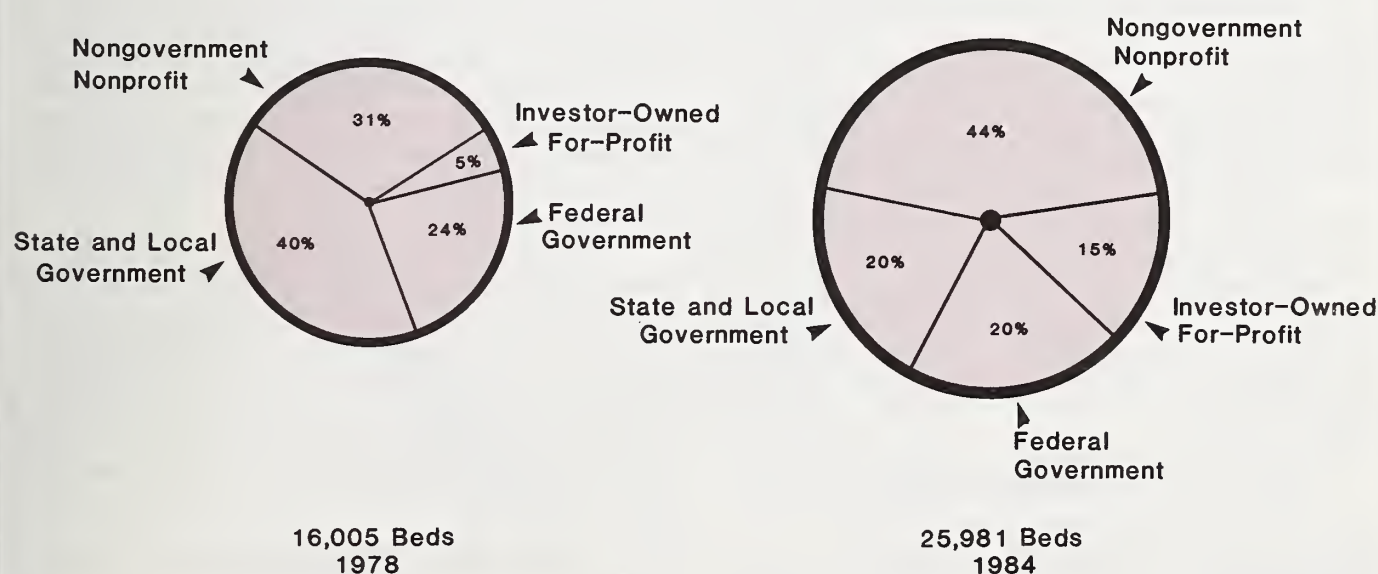


FIGURE 1. Control of hospital beds with services for alcoholism and other drug dependency.

SOURCE: Harwood et al. 1985.

## Development of the Alcohol Dependence Syndrome

In a series of studies, Wanberg and Horn and their colleagues (Horn and Wanberg 1969; Wanberg and Horn 1970, 1983; Horn et al. 1974, 1984; Wanberg et al. 1977) identified a multiple-syndrome diagnostic model through factor analytic techniques. Working with an initial item pool and larger samples, these authors succeeded in constructing the Alcohol Use Inventory. This instrument, consisting of 147 items and 16 scales, defines 6 dimensions that form patterns of alcohol use. In effect, Wanberg and Horn take the position that alcoholism is not a unitary phenomenon and that multiple syndromes are necessary to describe persons with alcohol-related problems.

Working with the Alcohol Use Inventory, Skinner (1981) developed the Alcohol Dependence Scale. Four scales from the Alcohol Use Inventory make up Skinner's Alcohol Dependence Scale: (1) loss of behavioral control, (2) psychophysical withdrawal symptoms, (3) psychoperceptual withdrawal symptoms, and (4) obsessive-compulsive drinking style. Skinner, in effect, through factor analytic techniques, identified a general factor that measures, in part, the alcohol dependence syndrome as outlined by Edwards and Gross (1976).

Hodgson et al. (1978) defined an alcohol dependence syndrome in terms of the following elements: (1) narrowing of the drinking repertoire, (2) salience of drink-seeking behavior, (3) increased tolerance to alcohol, (4) repeated withdrawal symptoms, (5) relief drinking, (6) compulsion to drink, and (7) readdiction liability.

The usefulness of the alcohol dependence syndrome concept lies in its potential for differentiating among people with alcohol-related problems with regard to severity of dependence. The hope of such differentiation, of course, is that it may lead eventually to meaningful predictions concerning individual treatment planning, individualized treatment interventions, and improved treatment outcome.

Research with the Severity of Alcohol Dependence Questionnaire (Edwards 1986), an instrument derived directly from the alcohol withdrawal syndrome concept, has

yielded empirical findings of significance. Stockwell et al. (1983) were able to provide evidence for one element of the syndrome, "narrowing of the drinking repertoire." Topham (1983) showed that degree of dependence was related to the speed with which sweating, shaking, craving, and morning drinking returned after relapse. Several studies have demonstrated relationships between measured level of dependence and desire for a drink, rapidity with which drinks are consumed, quantity of drinking, resistance to placebo-expectancy effects, and perception of withdrawal symptoms as cues for drinking (Hodgson et al. 1979; Rankin et al. 1980, 1982; Stockwell et al. 1982).

With regard to predicting resistance to abstinence as a treatment goal, Skinner and Allen (1982) found that all patients scoring high on the Alcohol Dependence Scale considered themselves to be alcoholics, and virtually all did not believe that they could cut down to a few drinks a day. In contrast, the majority of patients who scored low on alcohol dependence did not believe they were alcoholic and did believe they could cut down to a few drinks a day.

With regard to coexisting psychopathology, Skinner and Allen (1982) found significant relationships between scores on the Alcohol Dependence Scale and a host of measures of psychopathology. Two studies (Smail et al. 1984; Stockwell et al. 1984) found relationships between alcohol dependence scores and phobic anxiety. These studies suggest that clinicians should be alert to other problems as alcohol dependence increases.

The relationship of alcohol dependence to treatment goals is of interest. Edwards et al. (1983) reported that virtually all patients followed over an 11-year period who scored moderate to high on the measure of alcohol dependence could not engage successfully in nonproblem drinking.

Vaillant (1983), in the context of a longitudinal study that spanned many years, observed that appearance of only a small number of dependence symptoms predicted failure at moderate or nonproblem drinking. Polich et al. (1981), in their analysis of the Rand Corporation followup data, concluded that their results were consistent with Edwards' emphasis on alcohol dependence and suggested that nonproblem drinking decreased as the severity of dependence increased.

Perhaps the relationship between severity of dependence and treatment goals is best summarized by Miller and Hester (1980, p. 102): "The picture that emerges is clear: individuals who will become successful controlled drinkers show less resemblance to the classic diagnostic picture of alcoholism. They have fewer problems related to drinking and have had them for a shorter period of time, have fewer symptoms and less family history of alcoholism, and drink less."

## Other Approaches to Heterogeneity of Problem Drinkers

As mentioned earlier, Skinner (1981), through factor analysis of the Alcohol Use Inventory, identified an alcohol dependence factor. Skinner also identified three other

TABLE 2. *Number of clients in treatment, budgeted capacity, and utilization rate for drug abuse and alcoholism treatment units*

Type of unit	Number of clients	Budgeted capacity	Utilization rate (percent)
Drug abuse units			
Drug abuse only units	137,076	146,046	93.9
Combined units			
(Drug abuse portion)	36,403	50,243	72.3
Total	173,479	196,289	88.3
Alcoholism units			
Alcoholism only units	203,469	241,260	84.3
Combined units			
(Alcoholism portion)	86,464	103,955	83.2
Total	289,933	345,215	84.0

SOURCE: National Drug and Alcoholism Treatment Utilization Survey, September 1983.



factors: (1) perceived benefits of drinking (the person believes that alcohol facilitates social and mental functioning), (2) marital discord (drinking problems are intimately associated with marital difficulties), and (3) polydrug abuse (illicit drug use along with a gregarious drinking style). These factors correlate with clinic attendance, physical symptoms, and psychosocial problems.

Morey et al. (1984) through cluster analysis identified three types of drinkers as determined by severity of their alcohol problem, psychopathology, cognitive functioning, and social adjustment (see figure 2). Type A, early-stage problem drinkers, had evidence of drinking problems but not major symptoms of alcohol dependence. Type B, with affiliative, moderate alcohol dependence, were more socially oriented and tended to drink daily. Type C, schizoid, with severe alcohol dependence, were socially isolated binge drinkers with the most severe symptoms of alcoholism. This typology may well predict resistance to abstinence as a treatment goal, because Type A patients (early-stage problem drinkers) believed that they could cut down on their drinking and that moderation was a desirable goal. However, it is difficult to identify Type A patients. Types B and C believed that they could not cut down and that abstinence would be the only successful approach. For a compendium of diagnostic instruments, interested readers are referred to Lettieri et al. (1985). Babor and Lauerma (1986) have provided a comprehensive review of the numerous other systems for classifying alcoholics that have been proposed.

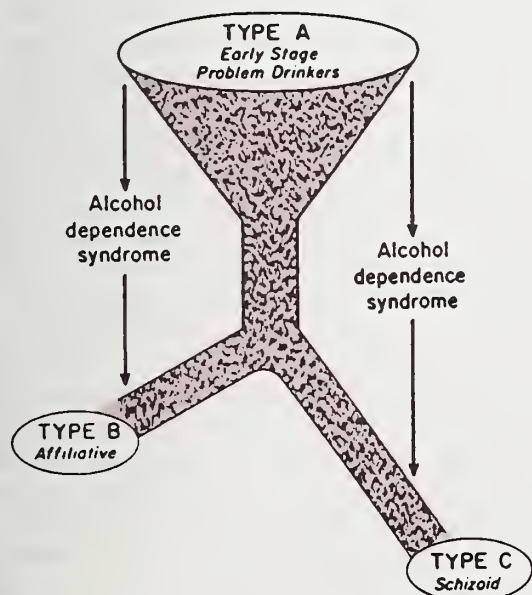


FIGURE 2. A speculative model for the classification of alcohol abuse.

SOURCE: Morey et al. 1984.

## Variability With Regard to Other Drug Abuse

Drug use and abuse among alcoholic treatment populations has increased sharply over the past decade. Sokolow and his colleagues (1981), in a study of 1,340 alcoholics in 17 New York State alcoholism treatment centers, found current other drug use in 46 percent of the patients. Freed (1973), in a review of the literature from 1925 to 1972, concluded that 20 percent of alcohol-dependent persons also use other addictive drugs. By 1977, however, a review by Carroll et al. suggested that between 60 and 80 percent of alcoholics use other drugs. Hesselbrock et al. (1985) found a lifetime incidence of other drug abuse in 45 percent of male primary alcoholics and 38 percent of female alcoholics. Schuckit (1985), in a study of the 577 alcoholics admitted to the San Diego Veterans Administration Medical Center between 1982 and 1984, found that 11 percent of the patients had a diagnosis of primary drug abuse and secondary alcoholism. Of Schuckit's primary alcoholic admissions, 53 percent had used marijuana, 23 percent stimulants, 14 percent cocaine, and 11 percent depressants.

These findings have important implications for clinical staffs who treat alcoholics. Clinical staffs must be prepared to alter their perceptions of and actions toward alcoholics who abuse other drugs because studies have shown that these patients are more impaired both physically and psychologically than are alcoholics who do not abuse other drugs. Schuckit (1985) reported many more childhood antisocial problems among primary drug abusers who abused alcohol than among primary alcoholics. Moreover, these patients showed more psychiatric hospitalizations, depressions, suicide attempts, and visits to mental health workers. Alcoholism counselors working with polydrug abuse alcoholic patients need to be alert to the increased likelihood of other serious problems and the necessity for individualized treatment interventions directed toward these.

Obviously, alcoholic patients who abuse other drugs will require information in treatment different from that given persons who do not abuse drugs. Given the high rates of other drug abuse in current treatment populations, lectures are essential on such topics as drug synergy; half-lives (amount of time necessary to metabolize one-half of initial dose); cross-tolerance; drug classifications; and effects on brain, lungs, heart, and other body systems and organs.

Because drugs can be more readily brought into alcoholism treatment centers and consumed there, numerous alcoholism treatment centers have implemented drug use detection systems.

## Psychiatric Disorders Among Alcoholic Treatment Populations

Alcoholic treatment populations vary considerably with regard to psychiatric problems. Halikas et al. (1983), through use of a systematic, structured interview, found evidence for psychiatric problems in 50 percent of a sample of 71 female alcoholics. The most common diagnosis was



affective disorder, with 24 percent showing unipolar disorder and 4 percent showing bipolar affective disorder. Ten percent of the patients had anxiety disorders of some kind. In addition, 6 percent had shown psychotic symptoms prior to treatment.

Hesselbrock and her colleagues (1985) also found high levels of psychiatric problems in alcoholism treatment patient samples. In her studies, 18 percent of the men and 38 percent of the women were seen as depressed, while 15 percent of the men and 29 percent of the women showed phobias. Five percent of the men and 9 percent of the women met criteria for panic disorder. Bedi and Halikas (1985) found a lifetime rate of affective disorder of 43 percent in alcoholic females and 29 percent in males.

In addition to influencing primary treatment, variations in primary diagnostic groups among alcoholics in treatment have implications for outcome results and planning for aftercare. Schuckit (1985) found that the best outcome results for a sample of 577 Veterans' Administration hospital patients were for primary alcoholics (78 percent of the sample), and the worst results were for primary antisocial personalities (7 percent of the sample). Primary antisocial personalities were younger, less well educated, and more likely to have reported secondary affective episodes, suicide attempts, and psychiatric hospitalizations. These people also reported patterns of drug abuse almost as intense as primary drug abusers. At followup, primary antisocial personalities with secondary alcoholism showed the worst outcome of any group; they had higher rates of police- and drug-related problems, using a weapon while drunk, and living on the streets. These results for primary, antisocial personality patients indicate that individualized treatment planning and interventions in both primary alcoholism treatment and aftercare must be the rule if outcome results are to be improved.

With regard to personality characteristics of alcoholics, Nerviano and Gross (1983) have summarized research in this area in terms of seven subtypes: (1) a chronic severe distress group, (2) passive aggressive sociopaths, (3) antisocial sociopaths, (4) acute reactive depressives, (5) a mixed-character dysphoric group, (6) a paranoid alienated group, and (7) a severely neurotic psychophysiological group. Some support for Nerviano and Gross' typology was provided by Bartsch and Hoffman (1985), who performed a cluster analysis on responses of alcoholics to the Millon Clinical Multiaxial Inventory.

Recognition of the variability in personality characteristics among alcoholics may have important implications for the clinical management of patients within given treatment programs as well as for patient assignment to treatment interventions, programs, and facilities. Moreover, post-treatment followup of certain types of patients may be more difficult—for example, patients who are younger, single, and of lower occupational status (Billings et al. 1985).

Because alcohol is a neurotoxin, it is not surprising to note that studies have shown neuropsychological deficits among alcoholism treatment populations and social drinkers (e.g., Parker and Noble 1977; Ryan et al. 1980). These

findings of impaired neuropsychological functioning have implications for the manner in which information is learned, stored, and retrieved by patients in treatment for alcoholism. Butters and Cermak (1980) have pointed to the possibility that long-term alcoholics may not spontaneously generate effective learning and memory strategies. Tarter and Parsons (1971) have demonstrated that alcoholics show difficulty on neuropsychological tests requiring concept formation and shifts in cognitive sets. These findings concerning learning, memory, and concept formation strategies may have important implications for how information is presented to alcoholics in lectures, group therapies, films, books, and other formats commonly employed in alcoholism treatment facilities. McCrady and Smith (1986) have recently explored implications of neuropsychological deficits for alcoholism treatment. Becker and Jaffe (1984) have shown impaired memory for treatment-relevant information in male alcoholics in inpatient treatment. Eckardt and Martin (1986) recommend that the cognitive capabilities of alcoholics be considered in the formulation of treatment plans, because there is evidence of brain dysfunction in a high proportion of detoxified alcoholics without organic brain syndrome and this makes neuropsychological assessment an important part of the overall clinical evaluation of alcoholic patients. However, the impact of cognitive impairment on alcoholism treatment outcome is not well understood at this time, and further research is needed in this area.

## THERAPEUTIC MODALITIES, CONTEXTS, AND METHODS

Although necessarily limited by cost-effectiveness considerations, alcoholism treatment has become increasingly multimodal and multidisciplinary. As is generally recognized, a comprehensive system of services is essential if the varying treatment needs of alcoholics are to be met. This comprehensive system of services includes at least the following: detoxification; inpatient rehabilitation; outpatient services, including clinic, day hospital, and partial hospital services; family treatment; aftercare; residential or supervised living services; and sobering-up services. These categories of service are not mutually exclusive.

### Detoxification

Research over the past decade has continued to show that detoxification can be accomplished in a variety of ways. Depending on the severity of withdrawal, the course of detoxification may be managed either medically or nonmedically. It is generally accepted that patients experiencing severe withdrawal symptoms and patients suffering from coexisting illnesses such as serious cardiac disease, hypertension, seizure disorders, and overt psychotic reactions will require medical management of detoxification in a medical setting. For patients experiencing mild to moderate withdrawal symptoms without coexisting medical problems, however, numerous studies suggest that detoxification may be accomplished safely in a nonmedical setting and without medication for a large number of alcoholics



(e.g., O'Briant et al. 1976/1977; Whitfield et al. 1978; Smith 1980; Den Hartog 1982; Diesenhaus 1982; Naranjo et al. 1983).

Gordis and Sereny (1981) argue that the important question concerning withdrawal and its management really relates to the possible impact of the withdrawal experience on successful outcome of rehabilitation treatment. These authors assert, "Withdrawal is but a small first step in rehabilitation. If the quality of withdrawal is unrelated to retention in treatment and successful rehabilitation, then it can be judged on cost and safety alone. If long-term outcome is somehow related to the withdrawal experience, then the cost of withdrawal treatment alone is a minor point" (Gordis and Sereny 1981, p. 44).

Unfortunately, as Gordis and Sereny point out, evidence is generally lacking on the possible relationship between withdrawal experience and subsequent success in modifying drinking behavior. One study (Fagan and Mauss 1978) did find that one-third of a predominantly socioeconomically deprived population did accept referral for rehabilitation treatment following detoxification. Smart and Gray (1978b) found that receiving medical evaluation and medication was related to acceptance and continuation in treatment as an outpatient. This effect was evident for lower middle-class and lower-class alcoholics. Reed and Mandell (1979), however, found no relationship between administration of chlordiazepoxide during withdrawal and completion of a 7-day hospital-based program.

With respect to alcoholics of higher socioeconomic classes, virtually nothing certain is known about the quality of withdrawal experience and subsequent modification of drinking behavior.

Studies are also needed of physician prescribing rules and behaviors within medical detoxification settings. Such studies are likely to reveal differences in the manner in which medical practitioners use psychoactive drugs in alcohol withdrawal. Some physicians appear to administer benzodiazepines or sedatives to all admissions to an alcoholism facility. Others seem to use medications only for patients experiencing severe withdrawal symptoms. Still others give medications mainly to prevent the onset of delirium tremens or to avoid seizures. Some may prescribe in order to make patients more comfortable during withdrawal in the belief that this action will increase the likelihood that patients will remain in the facility and accept rehabilitation treatment following detoxification. Obviously, empirical studies of differing physician motivations, beliefs, attitudes, and prescribing rules are needed to clarify the actual behavior of medical practitioners in medical detoxification settings. Surprisingly little is known with certainty as to what physicians actually do in such settings.

### Pharmacotherapies

There have been no dramatic developments in the pharmacotherapy of alcoholism since publication of the *Fourth Special Report* and *Fifth Special Report* (USDHHS 1981, 1984). Although pharmacotherapeutic agents of various kinds have continued to be used as adjuncts for limited

purposes, no specific, successful pharmacotherapy for altering long-term drinking behavior in alcoholics exists.

The complex issue of the effectiveness of disulfiram (Antabuse) was treated in considerable detail in both the *Fourth* and *Fifth Special Reports* (USDHHS 1981, 1984). The interested reader is urged to consult these documents. In general, however, as these reports make clear, disulfiram is no longer recommended for use alone in treating alcoholism, but it may be used as an adjunct to a comprehensive treatment regimen (Kwentus and Major 1979). As studies have shown, the effectiveness of disulfiram may be related to patient characteristics including age, motivation to remain sober, compulsivity, and ability to form dependent relationships. Moreover, in controlled studies disulfiram, when shown to be effective, has generally demonstrated only a small to modest effect. The usefulness of disulfiram, however, may be simply as a short-term influence over the decision to remain abstinent while the patient seeks to establish an initial program of recovery. Disulfiram for some patients may, in effect, constitute a way to "buy time" while they become further involved in treatment, pursue aftercare plans, or make contacts with self-help programs.

It is also possible that the willingness to take disulfiram is only a corollary of a strong motivation to quit drinking, and that individuals who are willing to take the drug daily would be likely to have a successful treatment outcome even if they did not take it.

The effectiveness of voluntary use of disulfiram in promoting abstinence has been challenged by a recent controlled, randomized, study involving 605 alcoholic men in nine clinics (Fuller et al. 1986). The patients were divided into three groups of about 200 men, and each group was randomly assigned to one of three treatment protocols: disulfiram in a pharmacologically effective dose plus counseling; disulfiram in an ineffective dose plus counseling; and counseling alone. Patients receiving disulfiram were told so, but they did not know whether they were receiving the effective or the ineffective dose, and, until the study was concluded, neither did the investigators. Thus this part of the study was "double-blinded" to avoid bias, and both disulfiram groups were presented with the same psychological threat of a disulfiram-alcohol interaction if they resumed drinking. After discharge from the hospital, the patients in all three groups were interviewed at regular intervals over a period of a year. Blood and urine alcohol tests were done during these followups to corroborate the patient's own reports of their alcohol consumption and compliance with Antabuse therapy. No significant differences were found in the three groups in percentage of total abstainers, time to first drink, employment, or social stability. Among the patients who drank, however, those receiving the pharmacologically effective dose of disulfiram reported significantly fewer drinking days than those receiving the ineffective dose. The investigators concluded that, although disulfiram in a pharmacologically effective dose did reduce the frequency of drinking in men who could not remain abstinent, it made no contributions to



sustained abstinence, delay of relapse, employment, and social stability beyond those provided by counseling alone.

Various methods have been tried with some success to increase patient compliance and, hence, disulfiram effectiveness. Azrin et al. (1982) reported a successful behavioral disulfiram assurance program that involved role playing and communication skills for some patients and a behavior therapy package for others. Liebson et al. (1978), working with heroin addicts who had secondary alcoholism, made receipt of methadone contingent upon disulfiram compliance. This procedure did result in higher rates of compliance. Wilson et al. (1984), as well as others, have employed subcutaneous disulfiram implants with improved compliance. Unfortunately, as Miller and Hester (1980) point out, serum blood levels with implants are unpredictable as are disulfiram/ethanol reactions. As a consequence, early enthusiasm for implants based upon positive initial outcome results in uncontrolled studies must be viewed cautiously.

Although initial reports of the effectiveness of lithium carbonate in alcoholism treatment indicated promise (Kline et al. 1974), subsequent research has provided mixed results. Pond et al. (1981) did not find reductions in drinking in alcoholics to whom lithium had been administered.

More recently, Fawcett et al. (1984) evaluated lithium carbonate therapy in a group of 84 volunteers who had also received other treatments for 3 weeks in two hospital alcoholism treatment programs, as well as attended AA during aftercare. Results did favor a group of patients who complied with the lithium medication regimen and showed blood levels at or above minimum therapeutic level ( $\geq 0.4$  m/q/L). These compliant patients with therapeutic blood levels of lithium were more likely to be abstinent at 6-month followup intervals than were all other groups studied.

Although the Fawcett et al. (1984) study is definitely of interest, it must be interpreted with caution. First, the numbers of patients in the four groups studied were small. By the 18-month followup, the results for the compliant patients with therapeutic blood levels of lithium were based on only eight patients. For noncompliant placebo controls, the number of patients at the 18-month followup was only seven. Second, there was a very high rate of major depression in these subjects, much higher than one expects to find in samples of alcoholics. At intake, 67 percent of the patients met criteria for major depression, and 88 percent met criteria for lifetime diagnoses of major depression. Moreover, 57 percent showed a lifetime course of recurrent unipolar depression. Obviously, these results for lithium, if reliable, may be applicable only to alcoholic patients with coexisting bipolar or unipolar affective disorder.

### Aversive Therapy

Presumably based on classical conditioning procedures in which conditioned stimuli are repeatedly paired with unpleasant unconditioned stimuli, aversion therapies have been used with specific treatment populations. In the case of alcoholism, conditioned stimuli are the sights, smells,

and tastes of alcoholic beverages, while the unconditioned stimuli have been nausea-producing drugs (chemical aversion therapy) or electric shock (electric aversion therapy).

Results concerning the efficacy of chemical aversion therapy have been both encouraging and discouraging (Lemere and Voegtlin 1950), poor to fair (Neuburger et al. 1981), modest (Neuburger et al. 1981), and good (Wiens et al. 1976; Wiens and Menustik 1983). As with most other approaches to alcoholism treatment, characteristics of patients undergoing chemical aversion therapy are important predictors of success. As a rule, patients who do well following chemical aversion therapy are married, socially stable, and of middle-class or higher socioeconomic status; they also have intact jobs and sufficient motivation to stay sober to expose themselves to an unpleasant treatment experience. The discouraging results referred to in the study by Lemere and Voegtlin (1950) were obtained with "charity" cases, while the poor to fair results of Neuburger et al. (1981) were associated with Medicare status, low socioeconomic class, and low educational level. Wiens and Menustik (1983) have demonstrated the increased efficacy of aversion therapy as a result of periodic booster treatments in aftercare.

Although chemical aversion therapy appears to be effective with highly motivated, good prognosis patients, electrical aversion therapy for alcoholics has not shown equivalent promise (e.g., Ewing 1984). In fact, Miller and Hester (1980, p. 36), following a review of the literature on electrical aversion therapy and abstinence, concluded that "electrical aversion therapy appears to be relatively ineffective in comparison to alternative methods."

Neither chemical aversion therapy nor electrical aversion therapy can be construed in terms of classical conditioning as originally proposed. The procedure seems to result in taste aversion rather than in a classically conditioned emotional or nausea response. In addition to chemical and electrical aversive therapy, a type of aversive therapy called covert sensitization therapy has been studied. In this procedure, verbally guided images concerning alcohol and drinking are associated with imagined nausea, vomiting, and other unpleasant experiences. Miller and Hester (1980, p. 42) point out that while the procedure is promising, present "research data are inadequate to reach firm conclusions regarding covert sensitization." However, numerous studies reviewed by Miller and Hester indicate that covert sensitization is more effective than no treatment. Nathan and Briddell (1977, pp. 340-341), however, have concluded that "aversive conditioning—electrical, chemical, or covert—has not been proven effective *in isolation* as a means of modifying or eliminating excessive drinking. When tested for therapeutic efficacy by themselves, neither electrical nor covert aversion led to significant changes in drinking behavior on either a short-term or long-term basis."

### Behavior Therapy

In addition to aversive therapies, other behavior therapy methods have been utilized. Some of these methods are as follows: behavioral self-control training including blood



alcohol discrimination training (teaching people to perceive accurately the level of alcohol in their bloodstream), video tape self-confrontation, relaxation training, systematic desensitization, extinction, social skills training, operant conditioning procedures including a community-reinforcement method, and cognitive-behavioral methods. Two comprehensive reviews of studies on these procedures are available to the interested reader. An early review by Nathan and Briddell (1977) and a recent review by Miller and Hester (1980) have provided summaries of research on these methods. In general, results suggest promise for some of these methods and problems with others. In particular, Hunt and Azrin's (1973) work on community-reinforcement approaches has shown interesting results. In Hunt and Azrin's study, two groups of alcoholics were studied. The experiment group received help from an experienced behavioral clinician in the community. The help consisted of assistance in finding employment, improvement in family and marital relations, enhancement of social skills, and restructuring of reinforcing social skills. The control group received standard hospitalization milieu therapy only. Results showed that the community-reinforcement group showed less time drinking, unemployed, away from home, or institutionalized than the control group. These results, however, were based upon only eight subjects in each condition.

Relaxation training and systematic desensitization in isolation appear to have little value in alcoholism treatment, but are probably effective as adjuncts for certain patients. A small effect of video tape confrontation is offset by a high patient dropout rate. Results with blood alcohol discrimination (Vogler 1982; Vogler and Bartz 1982) suggest that while it is of theoretical interest, it is of little practical importance in the treatment of alcoholism at this time. Behavioral self-control therapy, however, has received consistent support in a number of studies with certain types of problem drinkers. Investigations into cognitive-behavioral methods are presently underway.

### Counseling and Psychotherapy

Although individual and group counseling and some form of "psychotherapy" are widespread in the modern treatment of alcoholics, little is known with certainty about these procedures. Traditional dynamic psychotherapy has not been regarded as a treatment of choice for alcoholics, but it may be a useful adjunct for the treatment of co-existing psychopathology in some alcoholics. Treatment relies heavily on group methods (e.g., Blume 1985). McCrady and Sher (1983) have provided a recent comprehensive review of research on patient and treatment variables.

In contrast to classical, dynamic, insight-oriented psychotherapy, alcoholism counseling is directive, supportive, reality centered, focused on the present, short term, and oriented toward real world behavioral changes. Counselors vary in the importance they place on feelings expressed by the patients during therapy sessions. Counselors also differ in the degree of confrontation they use or will use with

resistant patients. Some counselors will use aggressive or even hostile confrontations with patients, while others regard such therapist behaviors as counterproductive (Wallace 1985b).

Although the benefits derived from confrontation with alcoholic patients may not be consistently productive, evidence exists that sharing information about the patient's condition in a realistic, straightforward, and nonthreatening manner may be beneficial. Kristenson et al. (1983) reported that persons given test results showing elevated liver enzymes associated with heavy drinking did modify their behavior accordingly. At followups lasting as long as 5 years, informed patients had lower mortality, incidence of illness and hospitalization, and absenteeism than a group of controls.

Although reviews of the effectiveness of psychotherapy (e.g., Hill and Blane 1967) and of psychological treatments (Emrick 1975) are often cited as disappointing, careful examination reveals that these reviews appear to have had little to do with the effectiveness of individual psychotherapy. Much of Hill and Blane's review appears to have dealt with studies concerning larger program evaluations, with group therapy, or with poorly and incompletely described treatment modalities that may have had little to do with individual psychotherapy as such. As Cartwright (1981) has pointed out, Emrick's review dealt largely with studies of medical and behavioral therapies including drug therapies, hypnosis, and aversive conditioning. One-quarter of the studies dealt with total program evaluation; less than 10 concerned group and marital counseling. Since few of Emrick's studies dealt with individual psychotherapy, empirical studies bearing directly on individual and group counseling or "psychotherapy" should be considered a high priority. Many programs include considerable amounts of individual counseling.

A study by McLachlan (1974) is a clear example of the type of research needed in this area of study. McLachlan investigated the degree of correspondence between the patient's conceptual level and the therapist's conceptual level. At level 1, the lowest conceptual level, persons are poorly socialized, egocentric, impulsive, and cognitively simple. At level 2, they are dependent on authority, compliant, and concerned with rules. At level 3, they are independent, questioning, and self-assertive. Persons at the highest conceptual level are interdependent, empathic, and cognitively complex. Patients were designated as either matched or mismatched to their group therapists in terms of measured conceptual level. Hence, a level 1 patient was considered matched when he got a therapist with a similar conceptual level and mismatched if he got a therapist at the highest conceptual level. The results clearly favored the matched patients, who showed a 70 percent recovery rate (abstinence), versus mismatched patients, who showed a 50 percent recovery rate.

Cartwright (1981) has discussed the fact that only a small fraction of studies of alcoholism treatment have dealt with the therapist's perspective. He cites the early study by Ends and Page (1957) as one of a few that actually compared



different therapeutic perspectives. Ends and Page compared groups treated by Mower's two-factor learning theory therapy, client-centered therapy, psychoanalytic therapy, and social discussions. The poorest outcome was for two-factor learning theory; the best outcome was for client-centered therapy. Psychoanalytic therapy was second, and social discussion third.

Pomerleau et al. (1978) compared behavioral self-control training to insight-oriented psychotherapy and found a significant total improvement rate of 72 percent at 12-month followup in the behavioral group versus 50 percent in the insight-oriented group.

Brandsma et al. (1980) compared patients randomly assigned to rational behavior therapy, insight-oriented therapy, AA, or an untreated control group. Both treated groups and AA participants had better outcomes than the untreated controls, and the treated groups did slightly better than the AA members. In a review of group therapy with alcoholics, Brandsma and Pattison (1986) found some evidence for effectiveness. However, abstinence or improvement rates varied from a low of 15 percent to a high of 53 percent.

An earlier paper by Rosenberg et al. (1976) is of interest. Working with counselor trainees, these investigators were able to show large differences in ability to keep patients in treatment. Differences were attributable to therapist behaviors because the characteristics of the patients of the successful counselors did not differ from the characteristics of patients of the unsuccessful counselors. What is needed is an extension of this study in which differences between successful and unsuccessful counselors are examined as well. Valle (1981), for example, has shown that when counselors are compared on levels of interpersonal functioning, counselors with higher levels of functioning have patients who show fewer relapses, fewer relapse days, and less use of alcohol during 2 years after treatment.

Given the crucial role that counselors and therapists of various therapeutic perspectives play in the treatment of alcoholism, it is evident that considerably more empirical study of counselor behaviors, styles, attitudes, beliefs, and personality characteristics is needed in the field of alcoholism treatment.

### Alcoholics Anonymous

Programs such as Alcoholics Anonymous, Al-Anon, and Alateen continue to provide critically needed, community-based support services for alcoholics and their families. While Alcoholics Anonymous is a program for alcoholics, Al-Anon is a separate program for the spouses, parents, adult children, siblings, and other concerned persons whose lives are closely tied to alcoholics. Alateen is a program for the teenage children of alcoholics. Large numbers of alcoholics achieve sobriety and maintain it for many years through Alcoholics Anonymous alone. Others recover through a combination of professional treatment services and membership in AA. Precisely how many people recover through AA alone or AA in conjunction with professional treatment services is not known with certainty. However, there is evidence that attendance at

AA meetings is positively correlated with the maintenance of abstinence (Gordis et al. 1981; Polich et al. 1981; Pettinati et al. 1982; Vaillant 1983).

Pettinati et al. (1982), in a 4-year followup study of 225 alcoholics treated in an inpatient program, found that regular attendance at AA meetings was significantly related to abstinence. Other posttreatment interventions were not related to abstinence. Vaillant et al. (1984), in an 8-year longitudinal study of 100 alcoholics, found a "striking association" between attendance at AA meetings and continued recovery.

An approach to evaluating the effectiveness of certain AA concepts in a treatment context has been provided by Alford (1980). Studying 56 alcoholic patients (27 men and 29 women) in an AA-oriented inpatient treatment setting, Alford found that 58 percent were abstinent at 6 months following treatment. This study, of course, provides only a partial test of AA effectiveness because it is addressed to AA concepts as applied in a treatment setting and not to the fellowship of AA.

Although many anecdotal reports attest to the effectiveness of AA, at present its effectiveness has not been scientifically documented (Glaser and Ogborne 1982; Miller and Hester in press). Conducting controlled evaluations of AA is difficult because of methodological problems. Research is hampered by the voluntary and informal nature of AA, absence of membership lists, and poor documentation; existing studies suffer from inadequate baseline assessment and followup (Glaser and Ogborne 1982). Many of the existing studies have evaluated AA not by itself but as one element of a complex treatment program, making it difficult to determine AA's independent contribution to outcome (Miller and Hester 1980).

A review of the literature on outcomes in AA suggests an abstinence rate between 26 percent and 50 percent at 1 year, which compares favorably with the results of other approaches (Miller and Hester 1980). AA may be optimal for a certain type of alcoholic; future research needs to identify the type of person for whom AA is the best approach (Glaser and Ogborne 1982).

AA membership changes continue to be reported through the fellowship's triennial survey. In the 1983 survey (AA World Services 1984), worldwide membership was reported as 1,351,793. U.S. membership was reported as 630,679, up from 476,000 in 1980. The percentage of women in the 1983 survey remained constant since 1980 at 30 percent. The proportion of people 30 years old and under increased from 14.7 percent in 1980 to 20 percent in 1983. The proportion of people reporting counseling agencies and treatment facilities as responsible for referral to their first AA meeting continues to rise from 19 percent in 1977 to 26 percent in 1980 to 31 percent in 1983. Finally, more persons with drug problems in addition to their alcohol problems are entering AA (31 percent of the membership).

Prior to the introduction of formal treatment programs for family members, the spouses, parents, and children of alcoholics had nowhere to turn for help, advice, and



support other than Al-Anon and Alateen. Spouses of alcoholics, particularly wives, were often regarded as neurotic and treated inappropriately in the mental health system. The stress of living with or near active alcoholism was not recognized, and psychological problems of spouses were regarded as intrapsychic in origin and treated accordingly. Due to the efforts of Al-Anon, attention came to be focused on family members as well as on the alcoholic within the family system.

Without question, AA, Al-Anon Family Groups, and Alateen are fellowship programs that have played and will continue to play major roles in community responses to alcoholism.

### Marital and Family Therapy

Alcohol problems affect and are affected by the patient's family situation. Marital and family therapy includes a variety of therapeutic techniques used by clinicians who share a conviction that disturbed family life plays a significant role in individual pathology and that treating the family will produce positive change. In some approaches, treatment targets not only the drinking and drinking-related behaviors of the patient but also the patterns of family communication and interaction.

Therapeutic approaches that involve the family have given encouraging results (Moos and Moos 1984), and controlled studies of marital or family therapy for alcoholics have found moderately better short-term outcomes than individual approaches (McCrary et al. in press). Alcoholics treated in joint hospitalization programs with their spouses showed more improvement after 4 years than did patients treated only with individual therapy or with joint therapy sessions with their spouses, but the differences were not significant (McCrary et al. 1982). At 4 years the subjects from the three groups were similar with respect to periods of abstinence, drinking history, and use of hospitalization and aftercare resources. Whereas more than three-fourths of the subjects showed short-term improvement at 6 months, less than one-third functioned consistently well over the 4 years. Findings suggest that a certain subpopulation of married alcoholics may benefit from intensive conjoint involvement and that involvement of the spouse may have an important short-term impact but no particular long-term advantage over individual treatment. In general, these studies by McCrary et al. (1986) and Moos and Moos (1984) have strongly supported the hypothesis that family dysfunction appears to be the result of alcoholism rather than the cause of it.

In another study comparing couples groups (in which the husband had begun outpatient alcoholism counseling) with individual treatment (O'Farrell et al. 1985), the behavioral marital therapy group had improved marital adjustment compared with couples in interactional therapy and individuals treated alone, although differences in drinking behavior were not statistically significant. However, the husbands in the behavior marital therapy group had fewer alcohol-involved days during treatment.

A recent study by McCrary et al. (1986) has compared the effectiveness of different types of spouse involvement

in alcoholism treatment. Alcoholics and their spouses were treated as outpatients with minimal spouse involvement, alcohol-focused spouse involvement, or alcohol-focused spouse involvement plus marital therapy. Although all subjects markedly reduced their drinking and reported increased life satisfaction, the best outcome was found in the marital therapy group. Alcoholics in this group improved more quickly, relapsed more slowly, were more likely to stay in treatment, and had better marital satisfaction.

A new approach under development, unilateral family therapy (Thomas and Santa 1982), is directed toward changing the behavior of an uncooperative family member by working with and providing therapeutic assistance to a cooperating member as a mediator.

In the past decade, clinicians have come to recognize family members as primary patients deserving of treatment in their own right, and not simply as adjuncts to treatment of the alcoholic. Modern treatment of spouses and children recognizes that the stress of living in an alcoholic family situation can, in some instances, have devastating effects upon the emotional and psychological health of family members. These problems must be addressed therapeutically whether or not alcoholic family members recover. Treatment of spouses, dependent children, and adult children of alcoholics have become central therapeutic issues; demand is increasing for therapeutic services for these groups independent of alcoholism treatment per se.

With growing recognition of the need for treatment of family members, regardless of the course of alcoholism in the alcoholic family member, evaluation of family therapy must begin to address questions other than the impact of such therapy on the drinking behavior of the alcoholic.

### FACTORS AFFECTING TREATMENT OUTCOME

The outcome of alcoholism treatment is a complex issue, one that involves many difficult questions. Emrick and Hansen (1983) point out that the outcome of treatment can be influenced by any and all of the following: patient characteristics, sample selection and attrition, patient experiences outside of and after treatment, duration of follow-up, type of outcome variables examined, analysis and interpretation of data, and a host of scientific methodological problems related to the conduct of outcome research (e.g., Emrick 1982; Emrick and Hansen 1985). Given these many sources of variability in treatment outcome results, it is not surprising to find striking differences in reported outcome statistics in the alcoholism treatment literature. When patients, programs, staffs, goals of treatment, community environments, definitions of successful outcomes, and conduct of research differ, it is obvious that no single outcome statistic could possibly describe the results of alcoholism treatment interventions.

Despite the complex issues involved in the evaluation of treatment, there is growing consensus that alcoholism treatment does work (Saxe et al. 1983). And in some instances, with particular patient populations treated with



particular methods, it works very well indeed. Increasing recognition of the effectiveness of treatment has led investigators to pose more sophisticated questions: For whom does alcoholism treatment seem not to work well and why? Can treatment results be improved for people who respond poorly to present treatments? Is it possible to match patients to treatment and increase effectiveness by doing so? Is alcoholism treatment cost-effective? These questions are considered in the following discussion of treatment outcome.

### Patient Characteristics as Factors in Outcome

Numerous studies have demonstrated the significance of patient characteristics in predicting outcome of treatment. As a rule, patients who are married, stably employed, free of severe psychological impairments, and of higher socioeconomic status respond most favorably to treatment (e.g., Baekeland 1977; Gibbs and Flanagan 1977; Neuburger et al. 1981; McLellan et al. 1983a). Gibbs and Flanagan (1977), in a review of 45 studies involving 55 different treatment groups, found several characteristics that were frequently but not always related to positive outcome. These were steady work history, marriage or cohabitation, higher status occupation, history of AA contact prior to treatment, higher social class, fewer arrests, and type of occupation regardless of status.

That such patient characteristics can influence treatment outcome is evident in a comparison of results for two programs serving very different populations. Patton (1979), in a followup study of employed, well-educated, largely middle- to upper middle-class alcoholics treated at the Hazelden Treatment Center in Minnesota, found a combined abstinence and improvement rate of 92 percent. At 18 months following treatment, 62 percent of the sample reported complete abstinence from alcohol for the entire 18-month period. Over the 18-month followup period, the followup response rate was 75 percent. Consideration of major possible sources of error in the Hazelden outcome suggests a lower bound of 50 percent for the 18-month abstinence rate. In effect, the reported 62 percent abstinence rate in Patton's study may be an overly optimistic estimate.

Gordis et al. (1981), working with a far more difficult patient population in which 71 percent were unemployed at the time of admission, 17 percent were on public assistance, and 50 percent had been treated for alcoholism elsewhere, reported an abstinence rate of 32 percent at 1 year. In contrast to the 75 percent followup rate at 18 months achieved by Patton (1979), Gordis et al. (1981) found that 45 percent of their patients were lost to followup before 30 days. Such dramatic differences in outcome results for these two programs serving very different populations are probably attributable to population rather than program differences. Costello (1980), for example, found a large correlation between scores on a measure of the treatment difficulty posed by patients and outcome of treatment. Treatment difficulty was a combined measure of social, biological, psychological, and drinking variables.

The more difficulty patients experienced in all these areas of functioning, the less likely they were to respond favorably to alcoholism treatment.

In summary, differences in response to treatment are often more readily attributable to the characteristics of patients served than to differences in program content.

### Contexts, Intensity, and Length of Treatment

It has long been recognized that not all alcoholics require formal treatment for alcoholism in order to recover. Many achieve recovery through community resources such as AA and other self-help groups, organized religions, and other means. As pointed out earlier, the 1983 survey of the membership of AA (Alcoholics Anonymous World Services 1984) reported that approximately 30 percent of its members come to the program through referral from counseling services and treatment facilities. This may mean that many members of AA may establish initial programs of abstinence without formal, professional treatment services. Precisely how many members of AA achieve initial abstinence without professional help of any kind is not known with certainty.

Just as alcoholics do not always need formal treatment to recover, those treated for alcoholism do not always require intensive treatment or longer-term inpatient treatment (Longabaugh et al. 1983). To define which alcoholics require more intensive treatment through inpatient or outpatient programs, or longer-term inpatient treatment, however, will require further research on treatment outcome.

A number of studies have involved comparisons of inpatient care with outpatient care (Pittman and Tate 1972; Wanberg et al. 1974; Mosher et al. 1975; Wilson et al. 1978). Other studies have compared inpatient care to less intensive forms of treatment such as partial hospitalization (Longabaugh et al. 1983) and day clinic (McLachlan and Stein 1982). Edwards et al. (1977) and Orford et al. (1976) have compared patients receiving intensive outpatient treatment to patients given advice only.

With the exception of Wanberg et al. (1974), studies of treatment context have not yielded differences in outcomes between patients treated in inpatient settings versus outpatient, partial hospitalization, and day clinic settings.

While these studies do show consistent results, there are both methodological and interpretive issues that indicate that conclusions and implications must be drawn cautiously. When continuous abstinence (the most scientifically rigorous measure of successful outcome) is examined, interpretation of the majority of these studies is complicated by high relapse rates. In the Mosher et al. (1975) study at 6-month followup, 82 percent of the outpatients had relapsed (i.e., failed to sustain abstinence) versus 77 percent of the inpatients. Wilson et al. (1978) reported relapse rates of 74 percent for both inpatients and outpatients at 15-month followup. Pittman and Tate (1972) reported relapse rates of 71 percent for outpatients and 78 percent for inpatients at 12-month followup. Stein et al. (1975) reported 4-month followup relapse rates of 64 percent for outpatients and 57 percent for inpatients. (It is



important to note that Stein et al.'s (1975) relapse rates do not necessarily reflect sustained abstinence since they are based upon the numbers of patients in various outcome categories at each followup time period. Hence, a patient categorized as abstinent at 4-month followup could be drinking pathologically at 13-month followup and vice versa.) McLachlan and Stein (1982) reported relapse rates of 67 percent for both outpatients and inpatients at 12-month followup. Longabaugh et al. (1983) reported 6-month relapse rates of 57 percent with these rising to 77 percent at 24-month followup (Fink et al. 1985). Edwards et al. (1977) reported that brief advice was presumably as effective as intensive treatment, but at 2-year followup (Orford et al. 1976), the relapse rate was 100 percent. As Orford et al. (1976) reported, the majority of men regardless of whether they had been in the "advice" or the treatment group drank within a few weeks of their initial consultation. By 12-month followup, all but 8 of the 95 men had returned to drinking, and by the 2-year followup only 2 of 95 men showed sustained abstinence with these 2 returning to drinking shortly thereafter. Given the 100 percent relapse rate in this study, the conclusion that the Edwards et al. (1977) study showed that brief "advice" is as effective as intensive treatment is unwarranted. Rather, the Edwards et al. (1977) study showed that *neither* advice nor intensive treatment was effective in the hands of these particular clinicians when effectiveness was defined in terms of the rigorous measure of sustained, continuous abstinence from alcohol following treatment.

In general, the relatively high relapse rates observed in the majority of the particular treatment programs and populations utilized in these studies of different treatment contexts raise serious problems of interpretation. When neither treatment program being compared is particularly effective, it is not possible to draw meaningful generalizations about comparative *cost-effectiveness*, for other inpatient treatment programs and treatment populations in which successful outcomes of 50 percent or more have been reported (e.g., Patton 1979; Laundergan 1982; Neubuerger et al. 1982; Wiens and Menustik 1983; Pickens et al. 1985). As Schuckit et al. (1986, p. 151) have cautioned, "However, even after these—[many]—factors are determined, it is still possible that findings from one population (e.g., veterans, the military, outpatients, skid row groups, court referred people) will not generalize to another."

With regard to questions concerning length and intensity of treatment, some studies appear to show no difference while others find effects favoring longer treatment. Numerous studies have not shown differences in treatment outcome as a result of length of treatment (e.g., Willems et al. 1973; Mosher et al. 1975; Page and Schaub 1979; Miller and Hester 1980, 1986; Emrick 1982; Powell et al. 1985).

Conversely, Welte et al. (1981) evaluated 756 patients at 3 and 8 months after inpatient treatment and found that patients who stayed in inpatient treatment longer were more likely to be abstaining or drinking less at followup. This improvement was greater among patients of low social stability. Bromet and Moos (1977) found that longer

lengths of stay appeared to decrease rehospitalizations in three of five alcoholism treatment facilities studied.

In a subsequent study, Finney et al. (1981) found significant positive correlations between length of stay in a halfway-house setting and abstinence, alcohol consumption, and rehospitalization at followup. Positive correlations between length of treatment and successful outcome have been reported by Armor et al. (1976), Smart (1978), and Smart and Gray (1978a). Kish et al. (1980) reported statistically significant differences at followup in sustained abstinence between alcoholic men with shorter stays and those with longer stays. Men who had stayed for shorter periods in an inpatient treatment setting had significantly more drinking episodes at followup (59 percent) than did men with longer stays (35 percent). Kish and Herman (1971) found differences in outcome associated with longer stays at the 1-year followup but not at the 2-year followup.

With regard to questions of context of treatment, length of stay, and intensity of treatment, it is likely that no general answer can be given. The considerable variability evident among alcoholics in psychiatric occupational, marital, family, psychological, and general social functioning indicates that variable lengths of stay will probably prove necessary. As pointed out previously, some alcoholics and problem drinkers will require no formal treatment, others may show improvement with minimal treatment (e.g., Miller and Baca 1983; Buck and Miller in press), others may require relatively brief stays in inpatient settings, and still others will require stays of a month or more in inpatient treatment if stable recovery is to be achieved. Research directed toward discovering explicit clinical criteria that can be used to determine how long individual patients will need to stay in inpatient and outpatient programs is needed.

### Patient-Treatment Matching

Given the necessity for a comprehensive system of alcoholism services and the need for variable lengths of stay in facilities offering such services, it does not appear fruitful to continue to pose questions in terms of one service versus another (e.g., inpatient versus outpatient) or one length of stay versus another (e.g., minimal treatment versus longer-term treatment). The considerable heterogeneity among alcoholic persons suggests that a person with one set of personal and situational characteristics may respond favorably to one type of treatment or setting but unfavorably to another. Such possible differential response to varying treatments has led to an interest in patient-treatment matching (Miller and Hester in press).

In the broadest meaning of the term, matching of patients to treatments occurs when individual treatments are administered in an effort to alleviate problems identified through clinical assessments. Many alcoholism treatment programs, including those that offer a single, common core program to all patients, provide this type of patient-treatment matching. Hence, depressed patients in a typical alcoholism rehabilitation program are usually referred for psychiatric evaluation and, if necessary, for



treatment with antidepressant medications. Patients who show a bipolar depression in addition to their alcoholism are stabilized with lithium as they complete their alcoholism rehabilitation program. Similarly, patients with anxiety disorders may be given relaxation training, desensitization therapy, or appropriate medications (e.g., low-dose antidepressant therapy in the case of panic disorder). Formal research on patient characteristics and response to treatment is an attempt to improve on this type of clinical patient-treatment matching by giving it a more rigorous empirical basis.

Formal research on patient-treatment matching may involve one or more of the following treatment components: therapeutic process, treatment regimen, treatment format, treatment setting, and treatment philosophy. Conceptual issues in patient-treatment matching have been discussed by Glaser (1980), Glaser and Skinner (1981), Finney and Moos (1986).

Research on patient characteristics and response to particular treatments has provided interesting hypotheses but is still far from conclusive. Moreover, many of the characteristics that have been related to one treatment in a particular study are clearly related to other treatments in other studies. For example, there have been a number of studies of patient characteristics and response to disulfiram treatment. These studies have shown that favorable responders tend to be older, socially stable, less depressed, more motivated, married, and more compulsive (Baeke-land et al. 1971; Fuller and Roth 1979; Azrin et al. 1982). Unfortunately, many, if not most, of these characteristics have been shown to be related to favorable response to *any* treatment, not just disulfiram therapy. For example, patients responding well to other drug aversion therapy are also older, socially stable, married, and motivated. The same set of patient characteristics describes favorable responders to inpatient rehabilitation treatment (e.g., Welte et al. 1981).

In order to show that particular characteristics are *differentially* related to different treatments, it is necessary to vary patient characteristics and treatments simultaneously. That is, one must study the responses of patients with varying characteristics to two or more treatments. These differential patient-treatment matching studies are rare. However, McLellan and his colleagues have contributed several studies in this regard.

In the first study, McLellan et al. (1983a) studied the responses to treatment of 460 alcohol-dependent and 282 drug-dependent patients treated in 6 different programs in the Veterans' Administration treatment network during 1978. The six programs were as follows: (1) Alcohol Therapeutic Community (60-day inpatient), (2) Fixed-Interval Drinking Decisions, (3) Combined Alcohol and Drug Program (60-day inpatient for alcoholics and drug addicts treated together), (4) Alcohol Outpatient, (5) Drug Abuse Therapeutic Community, and (6) Methadone Maintenance. When data were analyzed in terms of an addiction severity index, no significant differences were found. However, use of a measure of severity of psychiatric disturbance developed in an earlier study (McLellan et al.

1980) resulted in several interesting patient-treatment matches. Although patients with low severity of psychiatric problems did well in either inpatient or outpatient programs, patients with high severity of psychiatric problems did poorly no matter what treatment they received. The most interesting findings concerned those with middle-range severity of psychiatric problems. For patients with midrange psychiatric problems who also had greater employment or family problems, outpatient treatment led to worse outcomes than inpatient treatment. Patients with midrange psychiatric problems who also had legal problems tended to do less well in the two inpatient programs.

In a later prospective study, McLellan et al. (1983b) matched patients to their six treatment programs on the basis of findings from their first retrospective study. Using measures of psychiatric severity as well as measures of employment, family, and medical severity, the investigators succeeded in matching 53 percent of a new sample of 510 alcohol- and drug-dependent patients to appropriate treatments. Of the remaining 47 percent of the patients, 27 percent were mismatched to the appropriate treatment program because of lack of bed availability, 13 percent were mismatched because of the patient's refusal to accept a particular program assignment, and 7 percent of the mismatches stemmed from simple assignment errors or clinical staff disagreement with research decisions to assign patients to particular treatment programs.

The effects of matching patients to appropriate treatments were evident in some of McLellan et al.'s outcome measures. Matched alcohol-dependent patients from the low and midrange psychiatric severity groups were rated as significantly more motivated for treatment, stayed in treatment longer (60 days versus 50 days), and had a higher proportion of favorable discharges than did mismatched patients (33 irregular discharges versus 43 irregular discharges). Moreover, the matched alcohol-dependent patients showed significantly better 6-month outcomes concerning employment, medical condition, drug use, legal status, and family relations. In all, matched alcohol-dependent patients showed better outcomes on 17 of 19 followup comparisons.

In summary, the work by McLellan et al. (1980, 1983a, b) demonstrated two things. *First, even without patient-treatment matching procedures, alcoholism treatment was effective.* Alcohol-dependent patients who stayed in treatment for at least 15 days showed decreases of 67 percent in their drinking, reductions of 38 percent in family problems, reductions of 61 percent in psychiatric problems, and an increase of 92 percent in earned income 6 months after treatment. *Second, effectiveness of treatment was improved by matching patients to the most appropriate treatments.* The overall outcome of the matched patients (averaged across all criteria) was 19 percent better than that of the mismatched patients.

With regard to severity of impairment, hypotheses concerning length of stay have also been proposed. One might expect that more severely impaired alcoholics would do better in longer term treatment programs. However, one direct test of the hypothesis that alcoholics who are more



severely impaired neuropsychologically would respond better to longer lengths of stay was not confirmed (Walker et al. 1983). And in McLellan et al.'s (1983a,b) studies, alcoholics who were severely impaired psychiatrically did poorly in all types of treatment programs studied.

Despite these early discouraging findings, it is possible that as more is learned about alternative counseling and learning strategies with more severely impaired alcoholics (particularly the neuropsychologically impaired), new treatment methods developed specifically for this group may enhance outcomes (e.g., Goldman et al. 1985; McCrady and Smith 1986).

### Aftercare Services

It is widely accepted among alcoholism treatment professionals that aftercare services are a critical component of comprehensive alcoholism treatment services. A continuum of care including aftercare services is considered essential because of the relatively long period of recovery that many alcoholics appear to need and the high probability of relapse noted among alcoholics who leave treatment systems early. Walker et al. (1983) provide some empirical support for these traditional views of alcoholism treatment professionals. In a study of 245 male veterans grouped according to neuropsychiatric functioning, Walker and his colleagues found the strongest relationships were between aftercare involvement and treatment outcome. Patients who attended weekly aftercare groups for 9 months following hospitalization were three times more likely to remain abstinent than patients who dropped out of aftercare (70.2 percent versus 23.4 percent). These results are consistent with Costello's review of 23 2-year followup studies. The provision of an aggressive outpatient followup or aftercare was one of seven characteristics that distinguished successful from unsuccessful programs (Costello 1975). Further correlational analysis by Costello (1980) also supported clinicians' views on the importance of aftercare services.

Cronkite and Moos (1984), in a study of 332 alcoholic patients, found a tendency for more married men to have received outpatient aftercare than unmarried men (50 percent versus 41 percent). Unmarried women, in contrast, were more likely to have received outpatient aftercare than were married women (68 percent versus 44 percent). For men, receiving aftercare services was associated with better outcomes. Only 28 percent of the married men who had relapses had participated in outpatient aftercare, and 54 percent of the married men who did not suffer relapses had received outpatient aftercare.

In general, then, available data do support the traditional view of the importance of aftercare services in alcoholism treatment. With regard to length of aftercare services, Siegel et al. (1984a) tracked 325 alcoholic patients who had received inpatient treatment. Patients were followed for a period of 2 years in terms of how much outpatient aftercare they had used during this time and if they had been readmitted to inpatient services. Patients who had received either no outpatient services or an average of up to 5.4

months aftercare were more likely to be readmitted to inpatient care than patients receiving longer periods of aftercare.

### Cost Analyses of Alcoholism Treatment

What do alcoholism services cost relative to other problems in the mental health sector? Siegel et al. (1984b) have reported comparative costs of services to alcoholics and other mental health patients in suburban Rockland County, New York. A group of 315 patients with a primary diagnosis of alcoholism was compared with a group of 516 patients with nonalcoholic psychiatric diagnoses with regard to services for a 2-year period. Although alcoholics represented the largest single diagnostic group in the cohort studied (39 percent), the cost of their care was only 22 percent of the total cost. Alcoholics had lower costs because they used cumulatively fewer inpatient days and received fewer days of the most costly outpatient services of full-day treatment. Siegel et al. (1984b, p. 504) concluded, "On the average, the cost to treat severe alcoholic patients is less than half the cost to serve nonalcoholic patients."

Costello and Hodde (1981) raised questions about how costs are distributed among system components and among individuals. Inpatient treatment accounted for 73 percent of the costs generated by 100 socially unstable men and women patients to a comprehensive alcoholism treatment system, but only 5 patients accounted for 48 percent of the total inpatient treatment costs of \$297,150 over the 4-year period (1972-1976). In fact, these 5 patients accounted for 38 percent of the total treatment system costs of \$406,060. Two of these five patients were still in an inpatient setting after 4 years and had generated costs of \$29,585 and \$31,025, respectively. The most costly patient accounted for \$53,560 in less than 3 years before being transferred to a nursing home. Costello and Hodde (1981, p. 91) concluded not only that costs were not distributed equally over patients, but also that for this population of socially unstable alcoholics, "outpatient service and aftercare were extremely difficult to implement."

Still another question arising from cost analyses of alcoholism treatment concerns cost-benefit analysis. Do the benefits derived from treating alcoholics balance or offset the costs? A large number of studies reviewed by Jones and Vischi (1979) justify an affirmative response to the question of cost-benefit analysis in alcoholism treatment. Brock and Boyajy (1978) reported a 40 percent reduction in outpatient care utilization after alcoholism treatment while Sherman et al. (1979) found a 27 percent reduction in inpatient and outpatient medical care costs at Kaiser Permanente in Southern California. Hunter (1978), in a study of the Arizona Health Plan, found reductions in posttreatment care costs. With regard to dollar savings, Hayami and Freebori (1981), in the context of a health maintenance organization (HMO), estimated a savings of \$0.40 for every \$1.00 spent on treatment. Holder and Hallan (1978), in a study of the health benefits program of the California Public Employees Retirement system, found an annual



savings of \$84 per person following alcoholism treatment initiation. The authors followed a group of 90 alcoholics and their families from the same health insurance program and reported an average annual reduction in total health care costs of \$864 per person (Holder and Hallan 1981).

Holder and colleagues (1985) examined the impact of alcoholism treatment on overall health care utilization and costs for individuals and families filing claims with the Aetna Life Insurance Company under the Federal Employees Health Benefit Program. On the average, families with at least one member filing a claim for alcoholism treatment during calendar years 1980–1983 used health care services and incurred costs at a rate about twice that of a comparison group consisting of a random sample of families who filed no alcoholism claims during that period. Average monthly health care costs for the two groups over this period were \$210 per person and \$107 per person, respectively.

The study also found a gradual rise in the overall health care costs and utilization for alcoholics during the 3 years preceding alcoholism treatment, with the most dramatic increase occurring in the 6 months before treatment. Total monthly costs increased from about \$150 per month 2 years prior to treatment to an average of more than \$450 per month during the 6 months prior to treatment and \$1,370 in the final pretreatment month.

After alcoholics started treatment, their health care costs dropped significantly and eventually reached approximately the level that existed several years prior to treatment. Their total monthly costs averaged \$294 during the first 6 months after treatment and declined to an average of \$190 per month by 2.5 to 3 years after treatment. The most significant drop in health care costs occurred for treated alcoholics under the age of 45.

Using a variety of forecasting techniques, the project estimated that the average alcoholic's treatment cost could be offset by reductions in other health care costs within 2 to 3 years following the start of treatment.

Although sufficient empirical data are available to show that alcoholism treatment makes good sense from a cost-benefit perspective, data bearing on cost-effectiveness are less easily interpreted. At a micro level of analysis in which alternative treatments such as inpatient and outpatient care are delivered in a single hospital setting, it is reasonable to conclude that the costs associated with feeding and housing patients will be lower in particular outpatient treatment programs in comparison with particular inpatient programs.

However, because large health care systems' results may not mirror results at the level of the individual hospital, it is not possible to predict with certainty the impact of variations at the individual hospital level on large health care systems. For example, because inpatient and outpatient treatment may stand in a *complementary* rather than *substitutive* relationship at the large health care system level, increases in the provision of outpatient services could increase both the quality and the cost of care (Freiberg 1977). Hence, although outpatient costs are generally ac-

cepted as lower than inpatient costs, it does not necessarily follow that changing the mix of outpatient to inpatient services in all large health care systems will automatically result in substantial reductions in cost per unit of equivalent effectiveness. Numerous studies cited by Freiberg (1977) do not show reduced system costs as outpatient services are increased.

Despite these cautions, however, it is clear that alcoholism treatment not only is effective (Gottheil 1985), but also—because it has been shown to reduce total health care costs—probably constitutes an approach to cost containment generally in health care systems. Studies of cost-effectiveness are as yet inconclusive, but promising leads have been uncovered, particularly with regard to recent studies of patient-treatment matching (e.g., McLellan et al. 1983a, b). If treatment costs can be reduced and treatment effectiveness increased through patient-treatment matching, alcoholism treatment will show further gains in cost-effectiveness.

### Posttreatment Environment and Maintenance of Gains

The posttreatment environment, especially family characteristics and work settings, is important in the recovery process and may enable some alcoholics to attain essentially normal patterns of functioning. Moos and Finney (1983) designed strategies to recognize the extent of environmental factors external to treatment and their effect on treatment outcome. Environmental stressors, coping responses, and social resources had as much influence on the recovery process as did patients' treatment experiences and characteristics at intake combined, and posttreatment functioning of recovered alcoholics was similar to that of nonalcoholic control subjects (Moos et al. 1981; Billings and Moos 1983). Information from systematic assessments of extratreatment factors may help increase the effectiveness of treatment by identifying situations that increase the risk of relapse and by suggesting changes in coping patterns, family settings, and work settings.

Overall, about two-thirds of treated alcoholics improve, although reported success rates depend on whether the outcome indicator is abstinence, improved but not abstinent, or some other indicator (Saxe et al. 1983). One estimate of average short-term responses to treatment is that one-third of those treated become abstinent and one-third are improved but not abstinent (Miller and Hester 1980). Rates of abstinence at 1 year after treatment, a commonly used evaluative measure, typically range from 25 percent to 50 percent (Nathan in press). The lower rates are seen in poorly motivated, older, unemployed chronic alcoholics who are often in public treatment facilities. Higher rates are found among well-motivated, younger, employed, subchronic alcoholics treated in private facilities. At 3 years after treatment, the rates are generally half or less of the 1-year rates (Nathan in press).

Vaillant et al. (1983) have reported the results of an 8-year followup of a prospective study of alcoholism treatment. The duration of this study is twice that of any other



prospective study in the literature. Subjects were 100 inpatients who received 1 to 9 days of counseling and education and who attended AA meetings. At 8 years or at the time of death, 29 percent had achieved stable abstinence of at least 3 years' duration, 24 percent had intermittent alcoholism, and 47 percent had continuing serious alcohol problems. Premorbid social stability and sustained abstinence were major factors in good psychosocial outcome at 8 years, and premorbid social stability and AA attendance were independent contributors to sustained abstinence. The investigators suggest that these data and those from other longitudinal studies indicate that factors other than professional treatment itself have substantial effects on long-term outcome.

Marlatt (1984) has developed various cognitive assessment and intervention procedures designed to prevent relapse during the recovery or maintenance phase. These procedures emphasize the personal responsibility of alcoholics for their behavior and teach them techniques for coping with high-risk situations and dealing with urges and cravings. Research designed to test the theories underlying these procedures is under way.

A serious difficulty with many posttreatment assessment studies is their reliance on self-reports regarding alcohol consumption by the subjects. A study by Orrego et al. (1979) suggests that such reports should be regarded with much skepticism. From their study of outpatients with alcoholic liver disease, these investigators concluded that self-reports are very unreliable. Alcohol measurements were made on urine samples mailed by the 37 subjects daily for up to 6 months in order to check on the accuracy of their self-reports during periodic personal interviews. Patients who had alcohol in their urine were successful 52 percent of the time in convincing their physician that they had not been drinking, and 25 percent of patients with alcohol in their urine denied drinking at every interview. Only 17 percent of patients who had been drinking were consistently truthful about it. The investigators concluded that the personal interview should not be used to separate populations of abstainers and nonabstainers in the followup of alcoholic patients.

### Treatment Goals

Abstinence from alcohol as well as from other psychoactive drugs has been regarded as a major goal of treatment. Not only are today's treatment populations urged to abstain from drinking, they are also counseled to avoid minor tranquilizers; hallucinogens; central nervous system stimulants such as cocaine, amphetamines, and caffeine; narcotics; and all nonselective general depressant drugs. Of course, alcoholics with coexisting mental illnesses may be required to take medications directed at these additional problems, such as antidepressants, lithium, and phenothiazines. As a rule, however, alcoholism treatment is directed toward producing patients who neither drink alcohol nor take psychoactive drugs.

While there have been numerous reports of reduced drinking among some persons treated for alcoholism (e.g., Pattison et al. 1977), the case for questioning abstinence as

a desired goal of alcoholism treatment has rested upon a small number of highly influential studies. The study by Davies (1962), for example, has been regarded as a classic paper in this area by proponents of nonabstinence treatment goals and has been cited frequently. Davies reported that 7 "alcohol addicts" out of 93 patients sampled returned to sustained "normal drinking" over a period of 7 to 11 years. Edwards (1985), however, reinvestigated the fate of Davies' subjects and found that the majority of them could not be considered to be "normal drinkers," either during Davies' original followup or thereafter. The evidence gathered by Edwards indicated that five of Davies' seven subjects experienced significant drinking problems throughout the initial and subsequent followup periods, and that three of the five subjects also used psychotropic drugs heavily. The two remaining men (one of whom was never severely dependent on alcohol) did engage in trouble-free drinking over the entire period. In effect, only 2 percent of Davies' original sample of 93 patients appeared to be able to "return to normal drinking," and the evidence suggests that one of these two subjects was probably misdiagnosed because he was never severely dependent on alcohol.

A study by Vaillant (1983) provides a perspective on attempts by alcoholics to drink. This was a longitudinal study (1940–1980) on the natural history of alcoholism, using subjects in Harvard Medical School's Study of Adult Development. Vaillant reported that nonproblem drinking is not predictive of a favorable long-term outcome. Vaillant noted that when middle-aged alcoholics who had required detoxification attempted to return to asymptomatic drinking, their situation was analogous to driving a car without a spare tire—disaster was usually only a matter of time.

Finney and Moos (1981) reported on 131 patients who returned to their families after treatment in 1 of 5 residential, abstinence-oriented alcoholism treatment programs. Within the first 6 months, 36 had relapsed. Another 37 who had tried to drink moderately within 6 months of alcoholism treatment had a significantly higher relapse rate at the 2-year followup mark than did those who abstained for at least 6 months before beginning moderate drinking. Given the very high mortality rates for those alcoholics who continue to misuse alcohol, relapse is a most serious outcome (Barr et al. 1984).

Studies of inpatients given a broad-spectrum, moderation-oriented program in addition to hospital treatment have not yielded positive findings. Foy et al. (1984) studied 62 chronic alcoholics receiving broad-spectrum behavioral treatment for alcoholism as inpatients at a Veterans' Administration Medical Center. The subgroup of 30 that received additional training in nonproblem drinking skills had significantly fewer abstinent days and more abusive drinking days at 6 months' followup than did the 32 not given this training.

In another recent report, Helzer et al. (1985) examined the 5- to 7-year outcome for 1,289 diagnosed alcoholics (confirmed by record review) treated as inpatients or outpatients. Of the 83 percent of the sample who were followed, 1.6 percent were considered to be moderate



drinkers (up to six drinks a day), 15 percent had become totally abstinent, and 4.6 percent were mostly abstinent with occasional drinking. The investigators point out that the subjects were, however, likely to have been advised to stop drinking rather than to moderate their drinking. Helzer et al. concluded that the evolution to stable moderate drinking appears to be a rare outcome among alcoholics treated at medical or psychiatric facilities.

Pettinati et al. (1984) studied psychological functioning, as measured by the Minnesota Multiphasic Personality Inventory, in 61 alcoholics before they underwent inpatient treatment at 4 years' followup. Psychological functioning was most improved in those who maintained abstinence for a long time, compared with those who were abstinent with slips and those who were periodic drinkers. The investigators note that virtually no rehospitalization or subsequent treatment occurred among those who were able to maintain consistent and complete abstinence. Moreover, only 3 percent of the patients studied were able to engage in nonproblem drinking throughout the followup period.

In general, the bulk of clinical and scientific evidence appears to support the interpretation that once significant physical dependence has occurred; the alcoholic no longer has the option of returning to social drinking (Kissin and Hanson 1985); hence, abstinence is the most appropriate goal for alcoholic persons.

## SUMMARY

Alcoholism treatment services have increased in the 6 years from 1978 to 1984. More than 500,000 persons were reported to be in treatment on September 28, 1984, with 40,786 (8 percent) in an inpatient setting, 51,976 (10 percent) in a residential setting, and 447,649 (82 percent) as active outpatients. State and local government control of in-hospital treatment units decreased by 17 percent, while for-profit ownership of such units increased by 392 percent. Other drug abuse, alcohol or drugs, was recorded as a discharge diagnosis on 1.13 million (2.7 percent) of all discharges from short-term hospitals in 1983.

Continuing attention is being paid to the heterogeneity apparent among alcoholics, and various attempts to develop concepts and measurements appropriate to such heterogeneity have been apparent. The alcohol dependence syndrome concept has been researched extensively. Possible applications of this concept involve approaches to individualized treatment planning.

There have been no dramatic changes in pharmacotherapy for alcoholics. Interest continues in possible uses of disulfiram with some alcoholics as an adjunct to more comprehensive treatment. Lithium carbonate may constitute a useful therapy for some alcoholics, mainly those with coexisting affective disorder.

Detoxification of alcoholics can be accomplished safely and effectively in both social settings and medical settings. Severity of alcohol dependence and withdrawal symptoms, general medical condition, psychiatric features, and other factors determine which setting for detoxification is most appropriate.

Studies of inpatient and outpatient treatment indicate that some alcoholics do not require inpatient treatment. Patient-treatment matching, with patients assigned to different treatments on the basis of various characteristics that are correlated with outcome, continues to be of considerable interest. However, studies of inpatient and outpatient treatment indicate that it is not yet clear as to which alcoholics require inpatient treatment and which require outpatient treatment.

With regard to cost issues, the costs of treatment should be viewed in light of the current \$117 billion total economic care costs for alcoholism and problem drinking. All treatment expenditures, including a substantial portion for treatment of the medical consequences of alcoholism, are estimated at \$15 billion a year. Alcoholism treatment is effective for many persons. Favorable cost-benefit ratios that show reduced general health care expenditures in treated alcoholics indicate that alcoholism treatment is an effective means of containing health care costs throughout the health care system.

A problem that permeates all studies of treatment is the validity of self-reports. Research is needed to develop objective and reliable markers of treatment outcome.

Studies of treatment goals indicate that abstention from alcohol and other psychoactive drugs continues to be the most reasonable treatment goal for diagnosed alcoholics in light of current scientific and clinical information.

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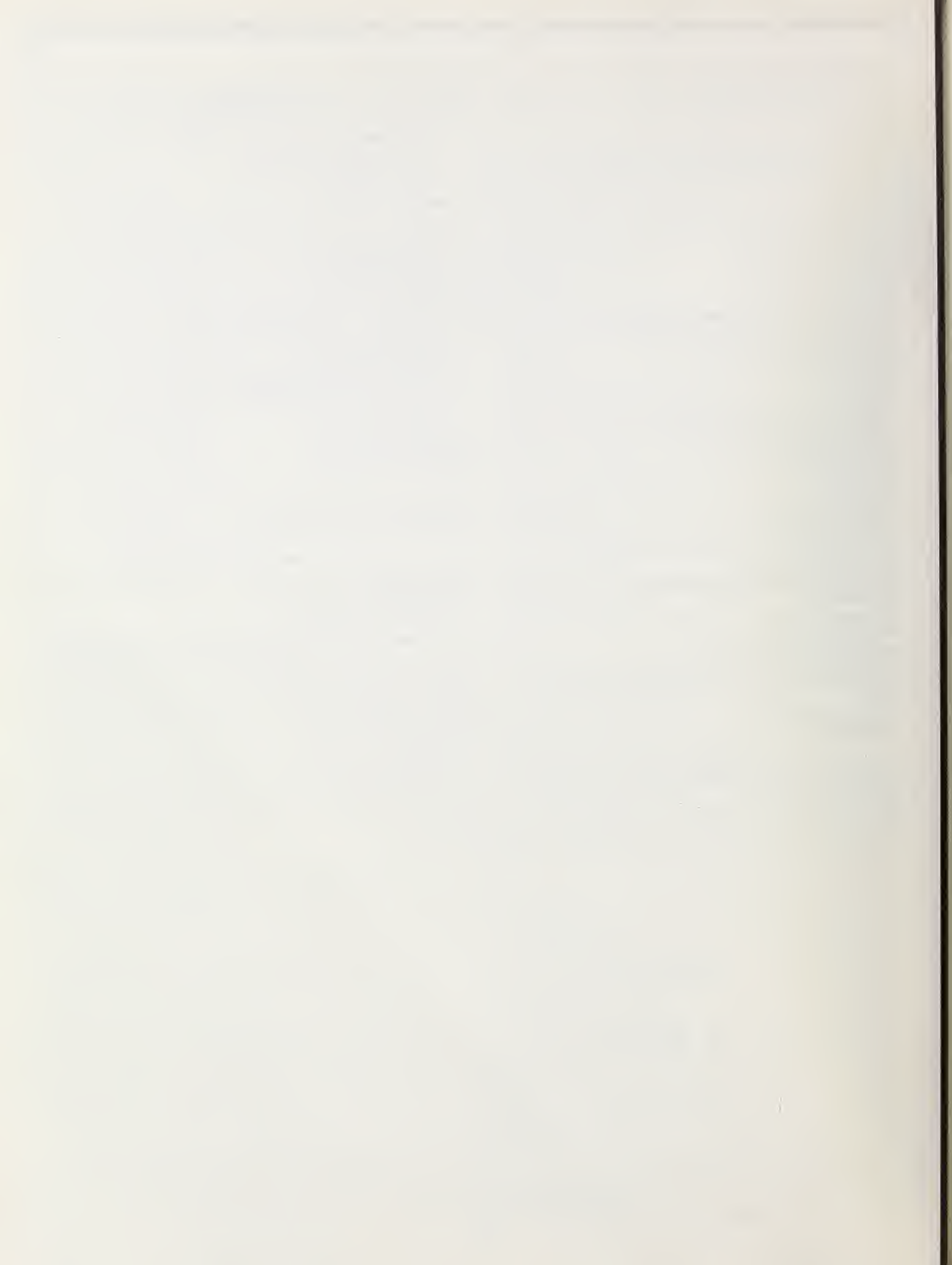
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